Al-201 – Autolmmune 12AP1/E5 -- Viventia Biotech AI-301 - Autolmmune 1964 -- Aventis AIDS vaccine - ANRS, CIBG, Hesed 20K growth hormone -- AMUR Biomed, Hollis-Eden, Rome, United 28P6/E6 -- Viventia Biotech Biomedical, American i-lome Products, 3-Hydroxyphthaloyl-beta-lactoglobulin -Maxygen 4-IBB ligand gene therapy airway receptor ligand -- IC Innovations 64-Cu MAb conjugate TETA-1A3 --- AJvW 2 -- Ajinomoto Mallinckrodt Institute of Radiology AK 30 NGF -- Alkermes 64-Cu MAb conjugate TETA-cT84.66 Albuferon -- Human Genome Sciences 64-Cu Trastuzumab TETA conjugate albumin - Biogen, DSM Anti-Infectives, Genentech Genzyme Transgenics, PPL Therapeutics, A 200 -- Amgen TranXenoGen, Welfide Corp. A10255 - Eli Liliy aldesleukin -- Chiron A1PDX - Hedral THerapeutics alefacept -- Biogen A6 - Angstrom Alemtuzumab aaAT-III -- Genzyme Allergy therapy -- ALK-Abello/Maxygen, Abciximab -- Centocor ALK-Abello/RP Scherer ABI.001 - Atlantic BioPharmaceuticals allergy vaccines -- Allergy Therapeutics ABT-828 - Abbott Alnidofibatide -- Aventis Pasteur Accutin Alnorine -- SRC VB VECTOR Actinohivin ALP 242 -- Gruenenthal activin -- Biotech Australia, Human Alpha antitrypsin -- Arriva/Hyland Therapeutics Immuno/ProMetic/Protease Sciences activin -- Curis Alpha-1 antitrypsin - Cutter, Bayer, PPL AD 439 – Tanox Therapeutics, Profile, ZymoGenetics, AD 519 – Tanox Adalimumab -- Cambridge Antibody Tech. Arriva Alpha-1 protease inhibitor -- Genzyme Adenocarcinoma vaccine – Biomira -- NIS Transgenics, Welfide Corp. Adenosine A2B receptor antagonists --Alpha-galactose fusion protein -Adenosine Therapeutics **Immunomedics** ADP-001 - Axis Genetics Alpha-galactosidase A -- Research AF 13948 - Affymax Corporation Technologies Afelimomab – Knoll Alpha-glucosidase - Genzyme, Novazyme AFP-SCAN - Immunomedics Alpha-lactalbumin AG 2195 – Corixa Alpha-L-iduronidase -- Transkaryotic agalsidase alfa -- Transkaryotic Therapies Therapies, BioMarin agalsidase beta -- Genzyme alteplase -- Genentech AGENT- Antisoma alvircept sudotox -- NIH AI 300 – Autolmmune ALX1-11 -sNPS Pharmaceuticals AI-101 - Teva Alzheimer's disease gene therapy -Al-102 - Teva

FIG. 1A

Anti-B4 MAb-DC1 conjugate -- ImmunoGen AM-133 -- AMRAD Anti-B7 antibody PRIMATIZED -- IDEC Amb a 1 immunostim conj. -- Dynavax Anti-B7-1 MAb 16-10A1 AMD 3100 - AnorMED -- NIS Anti-B7-1 MAb 1G10 AMD 3465 - AnorMED -- NIS Anti-B7-2 MAb GL-1 AMD 3465 – AnorMED -- NIS Anti-B7-2-gelonin immunotoxin -AMD Fab -- Genentech Antibacterials/antifungals --Amediplase - Menarini, Novartis Diversa/IntraBiotics AM-F9 Anti-beta-amyloid monoclonal antibodies --Amoebiasis vaccine Cambridge Antibody Tech., Wyeth-Ayerst Amphiregulin -- Octagene Anti-BLyS antibodies -- Cambridge anakinra -- Amgen Antibody Tech. /Human Genome Sciences analgesic -- Nobex Antibody-drug conjugates -- Seattle ancestim -- Amgen Genetics/Eos AnergiX.RA - Corixa, Organon Anti-C5 MAb BB5-1 -- Alexion Angiocidin -- InKine Anti-C5 MAb N19-8 -- Alexion angiogenesis inhibitors -- ILEX Anti-C8 MAb AngioMab - Antisoma anticancer cytokines -- BioPulse Angiopoietins -- Regeneron/Procter & anticancer matrix - Telios Integra Gamble Anticancer monoclonal antibodies - ARIUS, angiostatin -- EntreMed Angiostatin/endostatin gene therapy --Immunex anticancer peptides - Maxygen, Micrologix Genetix Pharmaceuticals Anticancer prodrug Tech. -- Alexion angiotensin-II, topical -- Maret **Antibody Technologies** Anthrax -- EluSys Therapeutics/US Army anticancer Troy-Bodies -- Affite -- Affitech Medical Research Institute anticancer vaccine -- NIH Anthrax vaccine Anti platelet-derived growth factor D human anticancers -- Epimmune Anti-CCR5/CXCR4 sheep MAb -- KS monoclonal antibodies -- CuraGen Biomedix Holdings Anti-17-1A MAb 3622W94 --Anti-CD11a MAb KBA -GlaxoSmithKline Anti-CD11a MAb M17 Anti-2C4 MAb -- Genentech anti-4-1BB monoclonal antibodies -- Bristol- Anti-CD11a MAb TA-3 -Anti-CD11a MAb WT.1 -Myers Squibb Anti-CD11b MAb -- Pharmacia Anti-Adhesion Platform Tech. -- Cytovax Anti-adipocyte MAb -- Cambridge Antibody Anti-CD11b MAb LM2 Anti-CD154 MAb -- Biogen Tech./ObeSys Anti-CD16-anti-CD30 MAb -- Biotest antiallergics -- Maxygen Anti-CD18 MAb -- Pharmacia antiallergy vaccine -- Acambis Anti-CD19 MAb B43 -Anti-alpha-4-integrin MAb Anti-angiogenesis monoclonal antibodies -- Anti-CD19 MAb -liposomal sodium butyrate conjugate -KS Biomedix/Schering AG

FIG. 1B

Anti-CD19 MAb-saporin conjugate –	Anti-CD4 MAb KT6
Anti-CD19-dsFv-PE38-immunotoxin -	Anti-CD4 MAb OX38
Anti-CD2 MAb 12-15 -	Anti-CD4 MAb PAP conjugate Bristol-
Anti-CD2 MAb B-E2 Diaclone	Myers Squibb
Anti-CD2 MAb OX34 –	Anti-CD4 MAb RIB 5-2
Anti-CD2 MAb OX54 –	Anti-CD4 MAb W3/25
Anti-CD2 MAb OX55 -	Anti-CD4 MAb YTA 3.1.2
Anti-CD2 MAb RM2-1	Anti-CD4 MAb YTS 177-9
Anti-CD2 MAb RM2-2	Anti-CD40 ligand MAb 5c8 Biogen
Anti-CD2 MAb RM2-4	Anti-CD40 MAb
Anti-CD20 MAb BCA B20	Anti-CD40 MAb 5D12 - Tanox
Anti-CD20-anti-Fc alpha RI bispecific MAb	-Anti-CD44 MAb A3D8
Medarex, Tenovus	Anti-CD44 MAb GKWA3
Anti-CD22 MAb-saporin-6 complex –	Anti-CD44 MAb IM7
Anti-CD3 immunotoxin —	Anti-CD44 MAb KM81
Anti-CD3 MAb 145-2C11 Pharming	Anti-CD44 variant monoclonal antibodies
Anti-CD3 MAb CD4lgG conjugate	Corixa/Hebrew University
Genentech	Anti-CD45 MAb BC8-I-131
Anti-CD3 MAb humanised – Protein Design	n, Anti-CD45RB MAb
RW Johnson	Anti-CD48 MAb HuLy-m3
Anti-CD3 MAb WT32	Anti-CD48 MAb WM-63
Anti-CD3 MAb-ricin-chain-A conjugate –	Anti-CD5 MAb Becton Dickinson
Anti-CD3 MAb-xanthine-oxidase conjugate	Anti-CD5 MAb OX19
, d	Anti-CD6 MAD
Anti-CD30 MAb BerH2 Medac	Anti-CD7 MAb-PAP conjugate
Anti-CD30 MAb-saporin conjugate	Anti-CD7 MAb-ricin-chain-A conjugate
Anti-CD30-scFv-ETA'-immunotoxin	Anti-CD8 MAb – Amerimmune, Cytodyn,
Anti-CD38 MAb AT13/5	Becton Dickinson
Anti-CD38 MAb-saporin conjugate	Anti-CD8 MAb 2-43
Anti-CD3-anti-CD19 bispecific MAb	Anti-CD8 MAb OX8
Anti-CD3-anti-EGFR MAb	Anti-CD80 MAb P16C10 IDEC
Anti-CD3-anti-interleukin-2-receptor MAb	Anti-CD80 MAb P7C10 ID Vaccine
Anti-CD3-anti-MOv18 MAb Centocor	Anti-CD8-idarubicin conjugate
Anti-CD3-anti-SCLC bispecific MAb	Anti-CEA MAb CE-25
Anti-CD4 idiotype vaccine	Anti-CEA MAb MN 14 – Immunomedics
Anti-CD4 MAb - Centocor, IDEC	Anti-CEA MAb MN14-PE40 conjugate –
Pharmaceuticals, Xenova Group	Immunomedics
Anti-CD4 MAb 16H5	Anti-CEA MAb T84.66-interleukin-2
Anti-CD4 MAb 4162W94 GlaxoSmithKli	ne conjugate
Anti-CD4 MAb B-F5 Diaclone	Anti-CEA sheep MAb KS Biomedix
Anti-CD4 MAb GK1-5	Holdings
FOR THE SECOND S	•

FIG. 1C

Anti-cell surface monoclonal antibodies	Anti-HIV antibody Epicyte
	anti-HIV catalytic antibody - Hesed Biomed
The state of the s	anti-HIV fusion protein Idun
	anti-HIV proteins Cangene
	Anti-HM1-24 MAb Chugai
1 (11) O1114 111 12	Anti-hR3 MAb
	Anti-Human-Carcinoma-Antigen MAb
Biomed	Epicyte
anti-EGFR immunotoxin IVAX	Anti-ICAM-1 MAb Boehringer Ingelheim
Anti-EGFR MAb Abgenix	Anti-ICAM-1 MAb 1A-29 Pharmacia
	Anti-ICAM-1 MAb HA58
	Anti-ICAM-1 MAb YN1/1.7.4
Title ZO: Tellin io Tio	Anti-ICAM-3 MAb ICM3 ICOS
Anti-EGFR MAb-DM1 conjugate	Anti-idiotype breast cancer vaccine 11D10
ImmunoGen	Anti-idiotype breast cancer vaccine
Anti-EGFR MAb-LA1 –	ACA14C5 —
Anti-EGFR sheep MAb KS Biomedix	Anti-idiotype cancer vaccine ImClone
Anti-FAP MAb F19-I-131	Systems/Merck KGaA ImClone, Viventia
Anti-Fas IgM MAb CH11	Biotech
Anti-Fas MAb DV 8	Anti-idiotype cancer vaccine 1A7 Titan
Anti-Fas MAb RK-8	
Anti-Flt-1 monoclonal antibodies ImClone	Anti-idiotype cancer vaccine TriAb - Titan
Anti-fungal peptides State University of	Anti-idiotype Chlamydia trachomatis
New York	vaccine
antifungal tripeptides BTG Anti-ganglioside GD2 antibody-interleukin-2	
Anti-ganglioside GDZ antibody-lineneukin-z	Novartis
fusion protein Lexigen	Anti-idiotype colorectal cancer vaccine
Anti-GM2 MAb Kyowa	Onyvax
Anti-GM-CSF receptor monoclonal	Anti-idiotype melanoma vaccine IDEC
antibodies AMRAD	Pharmaceuticals
Anti-gp130 MAb Tosoh	Anti-idiotype ovarian cancer vaccine ACA
Anti-HCA monoclonal antibodies	125
AltaRex/Epigen	Anti-idiotype ovarian cancer vaccine AR54 -
Anti-hCG antibodies Abgenix/AVI	- AltaRex
BioPharma	Anti-idiotype ovarian cancer vaccine CA-
Anti-heparanase human monoclonal	125 – AltaRex, Biomira
antibodies Oxford	Anti-IgE catalytic antibody Hesed Biomed
Glycosciences/Medarex	Anti-IgE MAb E26 Genentech
Anti-hepatitis C virus human monoclonal	Anti-IGF-1 MAb
antibodies XTL Biopharmaceuticals	anti-inflammatory – GeneMax
Anti-HER-2 antibody gene therapy	anti-inflammatory peptide BTG
Anti-herpes antibody Epicyte	anu-umanimatory pepudo - 510

FIG. 1D

Biomedix Holdings

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Anti-mu MAb -- Novartis anti-integrin peptides -- Burnha Anti-interferon-alpha-receptor MAb 64G12 -- Anti-MUC-1 MAb Anti-Nogo-A MAb IN1 Pharma Pacific Management Anti-nuclear autoantibodies -- Procyon Anti-interferon-gamma MAb -- Protein Anti-ovarian cancer monoclonal antibodies -Design Labs Anti-interferon-gamma polyclonal antibody - - Dompe Anti-p185 monoclonal antibodies - Advanced Biotherapy Anti-p43 MAb Anti-interleukin-10 MAb --Antiparasitic vaccines Anti-interleukin-12 MAb -Anti-interleukin-1-beta polyclonal antibody -- Anti-PDGF/bFGF sheep MAb -- KS **Biomedix** R&D Systems Anti-properdin monoclonal antibodies --Anti-interleukin-2 receptor MAb 2A3 Abgenix/Gliatech Anti-interleukin-2 receptor MAb 33B3-1 --Anti-PSMA MAb J591 -- BZL Biologics Immunotech Anti-Rev MAb gene therapy -Anti-interleukin-2 receptor MAb ART-18 Anti-RSV antibodies – Epicyte, Intracell Anti-interleukin-2 receptor MAb LO-Tact-1 Anti-RSV monoclonal antibodies --Anti-interleukin-2 receptor MAb Mikbeta1 Medarex/Medimmune, Applied Molecular Anti-interleukin-2 receptor MAb NDS61 Evolution/Medimmune Anti-interleukin-4 MAb 11B11 Anti-RSV MAb, inhalation --Anti-interleukin-5 MAb -- Wallace Alkermes/Medimmune Laboratories Anti-RT gene therapy Anti-interleukin-6 MAb - Centocor, Antisense K-ras RNA gene therapy Diaclone, Pharmadigm Anti-SF-25 MAb Anti-interleukin-8 MAb -- Xenotech Anti-sperm antibody -- Epicyte Anti-JL1 MAb Anti-Tac(Fv)-PE38 conjugate Anti-Klebsiella sheep MAb -- KS Biomedix Anti-TAPA/CD81 MAb AMP1 **Holdings** Anti-tat gene therapy Anti-Laminin receptor MAb-liposomal Anti-TCR-alphabeta MAb H57-597 doxorubicin conjugate Anti-TCR-alphabeta MAb R73 Anti-LCG MAb -- Cytoclonal Anti-tenascin MAb BC-4-I-131 Anti-lipopolysaccharide MAb -- VitaResc Anti-TGF-beta human monoclonal Anti-L-selectin monoclonal antibodies -antibodies -- Cambridge Antibody Tech., Protein Design Labs, Abgenix, Stanford Genzyme University Anti-TGF-beta MAb 2G7 -- Genentech Anti-MBL monoclonal antibodies --Antithrombin III -- Genzyme Transgenics, Alexion/Brigham and Women's Hospital Aventis, Bayer, Behringwerke, CSL, Anti-MHC monoclonal antibodies Anti-MIF antibody humanised - IDEC, Myriad Anti-Thy1 MAb Cytokine PharmaSciences Anti-Thy1.1 MAb Anti-MRSA/VRSA sheep MAb -- KS

FIG. 1E

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Anti-tissue factor/factor VIIA sheep MAb -- ARGENT gene delivery systems -- ARIAD Arresten KS Biomedix ART-123 -- Asahi Kasei Anti-TNF monoclonal antibodies arylsulfatase B -- BioMarin Centocor, Chiron, Peptech, Pharacia, Arylsulfatase B, Recombinant human --Serono BioMarin Anti-TNF sheep MAb -- KS Biomedix AS 1051 -- Ajinomoto Holdings ASI-BCL -- Intracell Anti-TNFalpha MAb - Genzyme Anti-TNFalpha MAb B-C7 -- Diaclone ATL-101 -- Alizyme atrial natriuretic peptide -- Pharis Anti-tooth decay MAb -- Planet BioTech. Aurintricarboxylic acid-high molecular antitumour RNases -- NIH weight Anti-VCAM MAb 2A2 -- Alexion autoimmune disorders -- GPC Anti-VCAM MAb 3F4 -- Alexion Biotech/MorphoSys Anti-VCAM-1 MAb Autoimmune disorders and transplant Anti-VEC MAb -- ImClone rejection -- Bristol-Myers Squibb/Genzyme Anti-VEGF MAb -- Genentech Tra Anti-VEGF MAb 2C3 Autoimmune disorders/cancer ---Anti-VEGF sheep MAb -- KS Biomedix Abgenix/Chiron, /CuraGen Holdinas Autotaxin Anti-VLA-4 MAb HP1/2 -- Biogen Avicidin -- NeoRx Anti-VLA-4 MAb PS/2 axogenesis factor-1 -- Boston Life Sciences Anti-VLA-4 MAb R1-2 Axokine -- Regeneron Anti-VLA-4 MAb TA-2 Anti-VRE sheep MAb -- KS Biomedix B cell lymphoma vaccine -- Biomira B7-1 gene therapy -Holdings BABS proteins -- Chiron ANUP -- TranXenoGen BAM-002 -- Novelos Therapeutics ANUP-1 -- Pharis Bav-16-9996 -- Bayer AOP-RANTES -- Senetek Apan-CH -- Praecis Pharmaceuticals Bay-39-9437 -- Bayer Bay-50-4798 -- Bayer APC-8024 -- Demegen BB-10153 -- British Biotech ApoA-1 -- Milano, Pharmacia BBT-001 -- Bolder BioTech. Apogen -- Alexion BBT-002 -- Bolder BioTech. apolipoprotein A1 -- Avanir BBT-003 -- Bolder BioTech. Apolipoprotein E -- Bio-Tech. General BBT-004 -- Bolder BioTech. Applaggin -- Biogen BBT-005 -- Bolder BioTech. aprotinin -- ProdiGene BBT-006 -- Bolder BioTech. APT-070C -- AdProTech BBT-007 -- Bolder BioTech. AR 177 -- Aronex Pharmaceuticals BCH-2763 -- Shire AR 209 - Aronex Pharmaceuticals, BCSF -- Millenium Biologix Antigenics BDNF - Regeneron - Amgen AR545C

FIG. 1F

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Becaplermin -- Johnson & Johnson, Chiron BST-3002 -- BioStratum Bectumomab – Immunomedics BTI 322 butyryicholinesterase -- Shire Beta-adrenergic receptor gene therapy --University of Arkansas C 6822 -- COR Therapeutics C1 esterase inhibitor -- Pharming Bi 51013 -- Behringwerke AG C3d adjuvant -- AdProTech BIBH 1 -- Boehringer Ingelheim CAB-2.1 -- Millennium BIM-23190 -- Beaufour-lpsen calcitonin - Inhale Therapeutics Systems, birch pollen immunotherapy -- Pharmacia bispecific fusion proteins -- NIH Aventis, Genetronics, TranXenoGen, Unigene, Rhone Poulenc Rohrer Bispecific MAb 2B1 -- Chiron calcitonin -- oral -- Nobex, Emisphere, Bitistatin BIWA 4 -- Boehringer Ingelheim Pharmaceutical Discovery Calcitonin gene-related peptide -- Asahi blood substitute - Northfield, Baxter Intl. Kasei -- Unigene BLP-25 -- Biomira BLS-0597 -- Boston Life Sciences calcitonin, human -- Suntory BLyS -- Human Genome Sciences calcitonin, nasal – Novartis, Unigene BLyS radiolabelled -- Human Genome calcitonin, Panoderm -- Elan calcitonin, Peptitrol -- Shire Sciences calcitonin, salmon -- Therapicon BM 06021 -- Boehringer Mannheim calin -- Biopharm BM-202 -- BioMarin BM-301 -- BioMarin Calphobindin I calphobindin I -- Kowa BM-301 -- BioMarin calreticulin -- NYU BM-302 -- BioMarin BMP 2 -- Genetics Institute/Medtronic-Campath-1G Campath-1M Sofamor Danek, Genetics Institute/ cancer therapy -- Cangene Collagenesis, Genetics cancer vaccine - Aixlie, Aventis Pasteur, Institute/Yamanouch BMP 2 gene therapy Center of Molecular Immunology, YM BMP 52 -- Aventis Pasteur, Biopharm BioSciences, Cytos, Genzyme, Transgenics, Globelmmune, Igeneon, BMP-2 -- Genetics Institute ImClone, Virogenetics, InterCell, Iomai, BMS 182248 --- Bristol-Myers Squibb Jenner Biotherapies, Memorial Sloan-BMS 202448 -- Bristol-Myers Squibb Kettering Cancer Center, Sydney Kimmel bone growth factors -- IsoTis Cancer Center, Novavax, Protein BPC-15 -- Pfizer Sciences, Argonex, SIGA brain natriuretic peptide – Cancer vaccine ALVAC-CEA B7.1 --Breast cancer -- Oxford Aventis Pasteur/Therion Biologics GlycoSciences/Medarex Breast cancer vaccine -- Therion Biologics, Cancer vaccine CEA-TRICOM -- Aventis Pasteur/Therion Biologics Oregon BSSL -- PPL Therapeutics Cancer vaccine gene therapy -- Cantab BST-2001 – BioStratum **Pharmaceuticals**

FIG. 1G

CETP vaccine -- Avant Cancer vaccine HER-2/neu -- Corixa Cancer vaccine THERATOPE -- Biomira Cetrorelix cancer vaccine, PolyMASC -- Valentis Cetuximab CGH 400 -- Novartis Candida vaccine – Corixa, Inhibitex CGP 42934 -- Novartis Canstatin -- ILEX CGP 51901 – Tanox CAP-18 -- Panorama CGRP -- Unigene Cardiovascular gene therapy -- Collateral CGS 27913 -- Novartis **Therapeutics** CGS 32359 -- Novartis carperitide -- Suntory Chagas disease vaccine -- Corixa Casocidin-1 -- Pharis CAT 152 -- Cambridge Antibody Tech. chemokines -- Immune Response CAT 192 -- Cambridge Antibody Tech. CHH 380 -- Novartis chitinase - Genzyme, ICOS CAT 213 -- Cambridge Antibody Tech. Chlamydia pneumoniae vaccine -- Antex Catalase-- Enzon **Biologics** Cat-PAD -- Circassia Chlamydia trachomatis vaccine -- Antex CB 0006 -- Celitech **Biologics** CCK(27-32)-- Akzo Nobel Chlamydia vaccine -- GlaxoSmithKline CCR2-64I -- NIH Cholera vaccine CVD 103-HgR -- Swiss CD, Procept -- Paligent Serum and Vaccine Institute Berne CD154 gene therapy Cholera vaccine CVD 112 -- Swiss Serum CD39 -- Immunex and Vaccine Institute Berne CD39-L2 -- Hyseq Cholera vaccine inactivated oral -- SBL CD39-L4 -- Hyseq Vaccin CD4 fusion toxin -- Senetek Chrysalin -- Chrysalis BioTech. CD4 lgG -- Genentech CI-782 -- Hitachi Kase CD4 receptor antagonists ---Ciliary neurotrophic factor - Fidia, Roche Pharmacopeia/Progenics CIM project -- Active Biotech CD4 soluble -- Progenics CL 329753 -- Wyeth-Ayerst CD4, soluble -- Genzyme Transgenics CL22, Cobra -- ML Laboratories CD40 ligand -- Immunex Clenoliximab -- IDEC CD4-ricin chain A -- Genentech Clostridium difficile antibodies -- Epicyte CD59 gene therapy -- Alexion clotting factors -- Octagene CD8 TIL cell therapy -- Aventis Pasteur CMB 401 -- Celltech CD8, soluble -- Avidex CNTF -- Sigma-Tau CD95 ligand -- Roche Cocaine abuse vaccine - Cantab, CDP 571 -- Celltech ImmuLogic, Scripps CDP 850 -- Celltech coccidiomycosis vaccine -- Arizo CDP 870 -- Celltech collagen -- Type! -- Pharming CDS-1 -- Ernest Orlando Collagen formation inhibitors -- FibroGen Cedelizumab -- Ortho-McNeil Cetermin -- Insmed FIG. 1H

Collagen/hydroxyapatite/bone growth factor CY 1747 -- Epimmune -- Aventis Pasteur, Biopharm, Orquest CY 1748 -- Epimmune Cyanovirin-N collagenase -- BioSpecifics Colorectal cancer vaccine -- Wistar Institute Cystic fibrosis therapy -- CBR/IVAX Component B, Recombinant -- Serono CYT 351 Connective tissue growth factor inhibitors -- cytokine Traps -- Regeneron cytokines - Enzon, Cytoclonal FibroGen/Taisho Cytomegalovirus glycoprotein vaccine -Contortrostatin Chiron, Aquila Biopharmaceuticals, contraceptive vaccine -- Zonagen Aventis Pasteur, Virogenetics Contraceptive vaccine hCG Cytomegalovirus vaccine live -- Aventis Contraceptive vaccine male reversible --**Pasteur IMMUCON** Cytosine deaminase gene therapy --Contraceptive vaccine zona pellucida --GlaxoSmithKline Zonagen DA-3003 -- Dong-A Copper-64 labelled MAb TETA-1A3 -- NCI DAB389interleukin-6 -- Senetek Coralyne DAB389interleukin-7 Corsevin M DAMP[^] -- Incyte Genomics C-peptide analogues -- Schwarz Daniplestim -- Pharmacia CPI-1500 -- Consensus darbepoetin alfa -- Amgen CRF -- Neurobiological Tech. DBI-3019 -- Diabetogen cRGDfV pentapeptide -DCC -- Genzyme CRL 1095 -- CytRx DDF -- Hyseq CRL 1336 -- CytRx decorin -- Integra, Telios CRL 1605 --- CytRx defensins -- Large Scale Biology CS-560 - Sankyo DEGR-Vila CSF -- ZymoGenetics Delmmunised antibody 3B6/22 AGEN CSF-G - Hangzhou, Dong-A, Hanmi CSF-GM - Cangene, Hunan, LG Chem Deimmunised anti-cancer antibodies --Biovation/Viragen CSF-M -- Zarix Dendroamide A CT 1579 - Merck Frosst Dengue vaccine -- Bavarian Nordic, Merck CT 1786 - Merck Frosst denileukin diftitox -- Ligand CT-112[^] -- BTG DES-1101 -- Desmos CTB-134L -- Xenova desirudin -- Novartis CTC-111 -- Kaketsuken desmopressin -- Unigene CTGF -- FibroGen Desmoteplase - Merck, Schering AG CTLA4-Ig -- Bristol-Myers Squibb Destabilase CTLA4-Ig gene therapy -Diabetes gene therapy – DeveloGen, Pfizer CTP-37 -- AVI BioPharma Diabetes therapy -- Crucell C-type natriuretic peptide -- Suntory Diabetes type 1 vaccine -- Diamyd CVS 995 - Corvas Intl. **Therapeutics** CX 397 - Nikko Kyodo

FIG. 11

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DiaCIM -- YM BioSciences EGF-P64k vaccine -- Center of Molecular Immunology dialytic oligopeptides -- Research Corp EL 246 -- LigoCyte Diamyd -- Diamyd Therapeutics elastase inhibitor -- Synergen DiaPep227-- Pepgen elcatonin -- Therapicon DiavaX -- Corixa Diphtheria tetanus pertussis-hepatitis B EMD 72000 -- Merck KGaA vaccine -- GlaxoSmithKline Emdogain -- BIORA emfilermin -- AMRAD DIR therapy -- Solis Therapeutics -Emoctakin -- Novartis DNase -- Genentech enamel matrix protein -- BIORA Dornase alfa -- Genentech Dornase alfa, inhalation -- Genentech Endo III -- NYU Doxorubicin-anti-CEA MAb conjugate endostatin – EntreMed, Pharis Enhancins -- Micrologix **Immunomedics** Enlimomab -- Isis Pharm. DP-107 -- Trimeris drotrecogin alfa -- Eli Lilly Enoxaparin sodium -- Pharmuka enzyme linked antibody nutrient depletion **DTctGMCSF** DTP-polio vaccine -- Aventis Pasteur therapy -- KS Biomedix Holdings Eosinophil-derived neutralizing agent – DU 257-KM231 antibody conjugate --EP-51216 -- Asta Medica Kvowa dural graft matrix -- Integra EP-51389 -- Asta Medica EPH family ligands -- Regeneron Duteplase – Baxter Intl. Epidermal growth factor -- Hitachi Kasei, DWP-401 -- Daewoong Johnson & Johnson DWP-404 -- Daewoong Epidermal growth factor fusion toxin --DWP-408 -- Daewoong E coli O157 vaccine -- NIH Senetek Epidermal growth factor-genistein -E21-R -- BresaGen Eastern equine encephalitis virus vaccine - EPI-HNE-4 -- Dyax EPI-KAL2 -- Dyax Echicetin – Epoetin-alfa - Amgen, Dragon Echinhibin 1 – Pharmaceuticals, Nanjing Huaxin Echistatin -- Merck Epratuzumab – Immunomedics Echitamine – EC-SOD -- PPL Therapeutics Epstein-Barr virus vaccine --Aviron/SmithKline Beecham, Bioresearch EDF -- Ajinomoto Eptacog alfa -- Novo Nordisk EDN derivative -- N!H EDNA -- NIH Eptifibatide -- COR Therapeutics erb-38 -Edobacomab -- XOMA Edrecolomab -- Centocor Erlizumab -- Genentech EF 5077 Efalizumab -- Genentech

FIG. 1J

EGF fusion toxin – Seragen, Ligand

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erythropoietin -- Alkermes, ProLease, Dong-Fas TR -- Human Genome Sciences A, Elanex, Genetics Institute, LG Chem, Felvizumab -- Scotgen Protein Sciences, Serono, Snow Brand, FFR-VIIa -- Novo Nordisk SRC VB VECTOR, Transkaryotic FG-001 - F-Gene FG-002 - F-Gene Therapies Erythropoietin Beta -- Hoffman La Roche FG-004 – F-Gene FG-005 - F-Gene Erythropoietin/Epoetin alfa -- Chugai Escherichia coli vaccine -- North American FGF + fibrin -- Repair Fibrimage -- Bio-Tech. General Vaccine, SBL Vaccin, Swiss Serum and fibrin-binding peptides – ISIS Innovation Vaccine Institute Berne fibrinogen -- PPL Therapeutics, Pharming etanercept -- Immunex fibroblast growth factor - Chiron, NYU, examorelin – Mediolanum Ramot, ZymoGenetics exonuclease VII fibrolase conjugate -- Schering AG F 105 -- Centocor Filgrastim -- Amgen F-992 -- Fomix filgrastim -- PDA modified -- Xencor Factor IX – Alpha Therapeutics, Welfide Corp., CSL, enetics Institute/AHP, FLT-3 ligand -- Immunex FN18 CRM9 -Pharmacia, PPL Therapeutics Factor IX gene therapy -- Cell Genesys follistatin -- Biotech Australia, Human Factor VII -- Novo Nordisk, Bayer, Baxter Therapeutics: follitropin alfa - Alkermes, ProLease, Intl. PowderJect, Serono, Akzo Nobel Factor VIIa -- PPL Therapeutics, Follitropin Beta - Bayer, Organon ZymoGenetics FP 59 Factor VIII – Bayer Genentech, Beaufour-Ipsen, CLB, Inex, Octagen, Pharmacia, FSH -- Ferring FSH + LH -- Ferring Pharming F-spondin -- CeNeS Factor VIII -- PEGylated -- Bayer fusion protein delivery system -- UAB Factor VIII fragments -- Pharmacia Research Foundation Factor VIII gene therapy -- Targeted fusion toxins -- Boston Life Sciences Genetics G 5598 -- Genentech Factor VIII sucrose formulation – Bayer, GA-II - Transkaryotic Therapies Genentech Gamma-interferon analogues -- SRC VB Factor VIII-2 -- Bayer VECTOR Factor VIII-3 -- Bayer Factor Xa inhibitors - Merck, Novo Nordisk, Ganirelix -- Roche gastric lipase -- Meristem Mochida Gavilimomab --Factor XIII -- ZymoGenetics Factors VIII and IX gene therapy -- Genetics G-CSF - Amgen, SRC VB VECTOR Institute/Targeted Genetics GDF-1 -- CeNeS GDF-5 -- Biopharm Famoxin -- Genset GDNF - Amgen Fas (delta) TM protein – LXR BioTech.

FIG. 1K

H5N1 influenza A virus vaccine -- Protein gelsolin -- Biogen Gemtuzumab ozogamicin -- Celltech Sciences Gene-activated epoetin-alfa -- Aventis haemoglobin -- Biopure haemoglobin 3011, Recombinant -- Baxter Pharma -- Transkaryotic Therapies Glanzmann thrombasthenia gene therapy -Healthcare haemoglobin crosfumaril – Baxter Intl. Glatiramer acetate -- Yeda glial growth factor 2 -- CeNeS haemoglobin stabilized -- Ajinomoto GLP-1 -- Amylin, Suntory, TheraTech, haemoglobin, recombinant -- Apex HAF -- Immune Response Watson Hantavirus vaccine GLP-1 peptide analogues - Zealand HB 19 **Pharaceuticals** HBNF -- Regeneron glucagon -- Eli Lilly, ZymoGenetics HCC-1 -- Pharis Glucagon-like peptide-1 7-36 amide -hCG -- Milkhaus Suntory hCG vaccine -- Zonagen Glucocerebrosidase -- Genzyme glutamate decarboxylase -- Genzyme HE-317 -- Hollis-Eden Pharmaceuticals Heat shock protein cancer and influenza **Transgenics** vaccines -- StressGen Glycoprotein S3 -- Kureha Helicobacter pylori vaccine -- Acambis, GM-CSF -- Immunex GM-CSF tumour vaccine -- PowderJect AstraZeneca/CSL, Chiron, Provalis Helistat-G -- GalaGen **GnRH** immunotherapeutic -- Protherics Hemolink -- Hemosol gp75 antigen -- ImClone hepapoietin -- Snow Brand gp96 -- Antigenics heparanase -- InSight GPI 0100 -- Galenica GR 4991W93 -- GlaxoSmithKline heparinase I -- Ibex Granulocyte colony-stimulating factor -heparinase III -- Ibex Hepatitis A vaccine -- American Biogenetic Dong-A Sciences Granulocyte colony-stimulating factor Hepatitis A vaccine inactivated conjugate Hepatitis A vaccine Nothav -- Chiron grass allergy therapy -- Dynavax Hepatitis A-hepatitis B vaccine --GRF1-44 -- ICN Growth Factor - Chiron, Atrigel, Atrix, GlaxoSmithKline hepatitis B therapy -- Tripep Innogenetics, ZymoGenetics, Novo Hepatitis B vaccine - Amgen, Chiron SpA, growth factor peptides -- Biotherapeutics Meiji Milk, NIS, Prodeva, PowderJect, growth hormone -- LG Chem Rhein Biotech growth hormone, Recombinant human --Hepatitis B vaccine recombinant -- Evans Serono Vaccines, Epitec Combiotech, Genentech, GT 4086 -- Gliatech GW 353430 -- GlaxoSmithKline Medlmmune, Merck Sharp & Dohme, Rhein Biotech, Shantha Biotechnics, GW-278884 -- GlaxoSmithKline Vector, Yeda H 11 -- Viventia Biotech

FIG. 1L

Hepatitis B vaccine recombinant TGP 943 -- HIV peptides -- American Home Products HIV vaccine -- Applied bioTech., Axis Takeda Genetics, Biogen, Bristol-Myers Squibb, Hepatitis C vaccine -- Bavarian Nordic, Chiron, Innogenetics Acambis, Genentech, Korea Green Cross, NIS, Oncogen, Protein Sciences Corporation, Hepatitis D vaccine -- Chiron Vaccines Terumo, Tonen Corporation, Wyeth-Hepatitis E vaccine recombinant --Ayerst, Wyeth-Lederle Vaccines-Malvern, Genelabs/GlaxoSmithKline, Novavax hepatocyte growth factor - Panorama, Advanced BioScience Laboratories, Bavarian Nordic, Bavarian Nordic/Statens Sosei Serum Institute, GeneCure, Immune hepatocyte growth factor kringle fragments -Response, Progenics, Therion Biologics, EntreMed Her-2/Neu peptides -- Corixa United Biomedical, Chiron Herpes simplex glycoprotein DNA vaccine - HIV vaccine vCP1433 -- Aventis Pasteur Merck, Wyeth-Lederle Vaccines-Malvern, HIV vaccine vCP1452 -- Aventis Pasteur Genentech, GlaxoSmithKline, Chiron, HIV vaccine vCP205 -- Aventis Pasteur HL-9 -- American BioScience Takeda HM-9239 -- Cytran Herpes simplex vaccine -- Cantab HML-103 -- Hemosol Pharmaceuticals, CEL-SCI, Henderson HML-104 -- Hemosol Morley HML-105 -- Hemosol Herpes simplex vaccine live -- ImClone Systems/Wyeth-Lederle, Aventis Pasteur HML-109 -- Hemosol HML-110 -- Hemosol HGF derivatives -- Dompe HML-121 -- Hemosol hIAPP vaccine -- Crucell Hib-hepatitis B vaccine -- Aventis Pasteur hNLP -- Pharis Hookworm vaccine HIC 1 host-vector vaccines – Henogen HIP-- Altachem Hirudins - Biopharma, Cangene, Dongkook, HPM 1 -- Chugai HPV vaccine -- MediGene Japan Energy Corporation, Pharmacia Corporation, SIR International, Sanofi-HSA -- Meristem HSF - StressGen Synthelabo, Sotragene, Rhein Biotech HSP carriers --Weizmann, Yeda, Peptor HIV edible vaccine -- ProdiGene HIV gp120 vaccine - Chiron, Ajinomoto, HSPPC-70 -- Antigenics HSPPC-96 -- pathogen-derived --GlaxoSmithKline, ID Vaccine, Progenics, VaxGen Antigenics HIV gp120 vaccine gene therapy -HSV 863 -- Novartis HIV gp160 DNA vaccine - PowderJect, HTLV-I DNA vaccine HTLV-I vaccine Aventis Pasteur, Oncogen, Hyland Immuno, Protein Sciences HTLV-II vaccine -- Access HU 901 -- Tanox HIV gp41 vaccine -- Panacos Hu23F2G - ICOS HIV HGP-30W vaccine -- CEL-SCI HIV immune globulin - Abbott, Chiron HuHMFG1

FIG. 1M

HuMax-IL15 -- Genmab HumaLYM -- Intracell HYB 190 -- Hybridon Human krebs statika -- Yamanouchi HYB 676 -- Hybridon human monoclonal antibodies --I-125 MAb A33 -- Celltech Abgenix/Biogen, Abgenix/ Corixa, Ibritumomab tiuxetan -- IDEC Abgenix/Immunex, Abgenix/Lexicon, IBT-9401 -- Ibex Abgenix/ Pfizer, Athersys/Medarex, IBT-9402 -- lbex Biogen/MorphoSys, CAT/Searle, IC 14 -- ICOS Centocor/Medarex, Corixa/Kirin Brewery, Idarubicin anti-Ly-2.1 -Corixa/Medarex, Eos BioTech./Medarex, Eos/Xenerex, Exelixis/Protein Design IDEC 114 -- IDEC IDEC 131 -- IDEC Labs, ImmunoGen/Raven, IDEC 152 -- IDEC Medarex/B. Twelve, MorphoSys/ImmunoGen, XTL **IDM 1 -- IDM** IDPS -- Hollis-Eden Pharmaceuticals Biopharmaceuticals/Dyax, iduronate-2-sulfatase -- Transkaryotic Human monoclonal antibodies --Medarex/Northwest Biotherapeutics. Therapies IGF/IBP-2-13 -- Pharis Medarex/Seattle Genetics IGN-101 -- Igeneon human netrin-1 -- Exelixis human papillomavirus antibodies -- Epicyte IK HIR02 -- Iketon IL-11 -- Genetics Institute/AHP Human papillomavirus vaccine -- Biotech IL-13-PE38 -- NeoPharm Australia, IDEC, StressGen Human papillomavirus vaccine MEDI 501 -- IL-17 receptor -- Immunex IL-18BP -- Yeda MedImmune/GlaxoSmithKline Human papillomavirus vaccine MEDI IL-1Hy1 -- Hyseq IL-1ß -- Celltech 503/MEDI 504 --IL-1ß adjuvant -- Celltech MedImmune/GlaxoSmithKline IL-2 -- Chiron Human papillomavirus vaccine TA-CIN -IL-2 + IL-12 -- Hoffman La-Roche Cantab Pharmaceuticals IL-6/sIL-6R fusion -- Hadasit Human papillomavirus vaccine TA-HPV --IL-6R derivative -- Tosoh Cantab Pharmaceuticals IL-7-Dap 389 fusion toxin -- Ligand Human papillomavirus vaccine TH-GW --IM-862 -- Cytran Cantab/GlaxoSmithKline human polyclonal antibodies -- Biosite/Eos IMC-1C11 -- ImClone imiglucerase -- Genzyme BioTech./ Medarex Immune globulin intravenous (human) -human type II anti factor VIII monoclonal Hoffman La Roche antibodies -- ThromboGenics immune privilege factor -- Proneuron humanised anti glycoprotein lb murine Immunocal -- Immunotec monoclonal antibodies -- ThromboGenics Immunogene therapy -- Briana Bio-Tech HumaRAD -- Intracell Immunoliposomal 5-fluorodeoxyuridine-HuMax EGFR -- Genmab dipalmitate -HuMax-CD4 -- Medarex

FIG. 1N

integrin antagonists -- Merck immunosuppressant vaccine -- Aixlie interferon (Alpha2) -- SRC VB VECTOR, immunotoxin – Antisoma, NIH Viragen, Dong-A, Hoffman La-Roche, ImmuRAIT-Re-188 - Immunomedics Genentech imreg-1 -- Imreg infertility -- Johnson & Johnson, E-TRANS interferon -- BioMedicines, Human Genome Influenza virus vaccine -- Aventis Pasteur, Sciences interferon (Alfa-n3)—Interferon Sciences **Protein Sciences** Intl. inhibin -- Biotech Australia, Human interferon (Alpha), Biphasix -- Helix Therapeutics Inhibitory G protein gene therapy interferon (Alpha)—Amgen, BioNative, Novartis, Genzyme Transgenics, INKP-2001 -- InKine Hayashibara, Inhale Therapeutics Inolimomab -- Diaclone insulin -- AutoImmune, Altea, Biobras, Systems, Medusa, Flamel, Dong-A, GeneTrol, Nastech, Shantha, BioSante, Bio-Tech. General, Chong Kun Dang, Emisphere, Flamel, Provalis, Rhein Wassermann, LG Chem, Sumitomo, Aventis, Behring EGIS, Pepgen, Servier, Biotech, TranXenoGen insulin (bovine) -- Novartis Rhein Biotech. insulin analogue -- Eli Lilly interferon (Alpha2A) interferon (Alpha2B) - Enzon, Schering-Insulin Aspart -- Novo Nordisk insulin detemir -- Novo Nordisk Plough, Biogen, IDEA interferon (Alpha-N1) -- GlaxoSmithKline insulin glargine -- Aventis interferon (beta) - Rentschler, GeneTrol, insulin inhaled – Inhale Therapeutics Meristem, Rhein Biotech, Toray, Yeda, Systems, Alkermes Daiichi, Mochida insulin oral -- Inovax interferon (Beta1A) - Serono, Biogen insulin, AeroDose -- AeroGen insulin, AERx -- Aradigm interferon (beta1A),inhale -- Biogen interferon (ß1b)-- Chiron insulin, BEODAS -- Elan interferon (tau) -- Pepgen insulin, Biphasix -- Helix insulin, buccal -- Generex Interferon alfacon-1 -- Amgen Interferon alpha-2a vaccine insulin, I2R -- Flemington insulin, intranasal -- Bentley Interferon Beta 1b -- Schering/Chiron, InterMune insulin, oral – Nobex, Unigene Interferon Gamma -- Boehringer Ingelheim, insulin, Orasome -- Endorex Sheffield, Rentschler, Hayashibara insulin, ProMaxx -- Epic interferon receptor, Type I -- Serono insulin, Quadrant -- Elan interferon(Gamma1B) -- Genentech insulin, recombinant -- Aventis Interferon-alpha-2b + ribavirin - Biogen, insulin, Spiros -- Elan insulin, Transfersome -- IDEA **ICN** insulin, Zymo, recombinant -- Novo Nordisk Interferon-alpha-2b gene therapy --Schering-Plough insulinotropin -- Sclos Interferon-con1 gene therapy – Insulysin gene therapy – **FIG. 10**

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IPF -- Metabolex interleukin-1 antagonists -- Dompe IR-501 -- Immune Response Interleukin-1 receptor antagonist -- Abbott ISIS 9125 -- Isis Pharmaceuticals Bioresearch, Pharmacia ISURF No. 1554 -- Millennium Interleukin-1 receptor type I -- Immunex ISURF No. 1866 - Iowa State Univer. interleukin-1 receptor Type II -- Immunex Interleukin-10 – DNAX, Schering-Plough ITF-1697 -- Italfarmaco IxC 162 -- Ixion Interleukin-10 gene therapy – interleukin-12 -- Genetics Institute, Hoffman J 695 -- Cambridge Antibody Tech., Genetics Inst., Knoll La-Roche Jagged + FGF -- Repair interleukin-13 -- Sanofi JKC-362 -- Phoenix Pharmaceuticals interleukin-13 antagonists -- AMRAD Interleukin-13-PE38QQR JTP-2942 – Japan Tobacce Juman monoclonal antibodies -interleukin-15 -- Immunex interleukin-16 -- Research Corp Medarex/Raven K02 -- Axys Pharmaceuticals interleukin-18 -- GlaxoSmithKline Keliximab -- IDEC Interleukin-1-alpha -- Immunex/Roche interleukin-2 -- SRC VB VECTOR, Keyhole limpet haemocyanin Ajinomoto, Biomira KGF -- Amgen KM 871 -- Kyowa Interleukin-3 -- Cangene **KPI 135 -- Scios** Interleukin-4 -- Immunology Ventures, **KPI-022** -- Scios Sanofi Winthrop, Schering-Plough, Kringle 5 Immunex/ Sanofi Winthrop, Bayer, Ono KSB 304 interleukin-4 + TNF-Alpha -- NIH KSB-201 -- KS Biomedix interleukin-4 agonist -- Bayer L 696418 -- Merck interleukin-4 fusion toxin -- Ligand Interleukin-4 receptor - Immunex, Immun L 703801 -- Merck Interleukin-6 - Ajinomoto, Cangene, Yeda, L1 -- Acorda L-761191 -- Merck Genetics Institute, Novartis lactoferrin – Meristem, Pharming, Agennix interleukin-6 fusion protein – lactoferrin cardio -- Pharming interleukin-6 fusion toxin – Ligand, Serono LAG-3 -- Serono interleukin-7 -- IC Innovations interleukin-7 receptor -- Immunex LAIT -- GEMMA LAK cell cytotoxin -- Arizona interleukin-8 antagonists -- Kyowa lamellarins -- PharmaMar/University of Hakko/Millennium/Pfizer Malaga interleukin-9 antagonists -- Genaera Iaminin A peptides -- NIH interleukins -- Cel-Sci lodine I 131 tositumomab -- Corixa lanoteplase -- Genetics Institute laronidase -- BioMarin ior EPOCIM -- Center of Molecular Lassa fever vaccine Immunology LCAT -- NIH lor-P3 -- Center of Molecular Immunology LDP 01 -- Millennium IP-10 -- NIH

FIG. 1P

Lyme disease vaccine -- Aquila LDP 02 -- Millennium Biopharmaceuticals, Aventis, Pasteur, Lecithinized superoxide dismutase --Symbicom, GlaxoSmithKline, Hyland Seikagaku Immuno, Medimmune LelF adjuvant -- Corixa Lymphocytic choriomeningitis virus vaccine leishmaniasis vaccine -- Corixa lymphoma vaccine - Biomira, Genitope lenercept -- Hoffman La-Roche Lenograstim - Aventis, Chugai LYP18 lys plasminogen, recombinant lepirudin -- Aventis Lysosomal storage disease gene therapy -leptin – Amgen, IC Innovations Leptin gene therapy -- Chiron Corporation Avigen leptin, 2nd-generation -- Amgen lysostaphin -- Nutrition 21 M 23 -- Gruenenthal leridistim -- Pharmacia M1 monoclonal antibodies -- Acorda leuprolide, ProMaxx -- Epic **Therapeutics** leuprorelin, oral -- Unigene MA 16N7C2 – Corvas Intl. LeuTech -- Papatin malaria vaccine -- GlaxoSmithKline, LEX 032 -- SuperGen AdProTech, Antigenics, Apovia, Aventis LiDEPT -- Novartis Pasteur, Axis Genetics, Behringwerke, lipase -- Altus Biologics CDCP, Chiron Vaccines, Genzyme lipid A vaccine -- EntreMed Transgenics, Hawaii, MedImmune, NIH, lipid-linked anchor Tech. - ICRT, ID NYU, Oxxon, Roche/Saramane, Biotech **Biomedical** liposome-CD4 Tech. -- Sheffield Australia, Rx Tech Malaria vaccine CDC/NIIMALVAC-1 Listeria monocytogenes vaccine malaria vaccine, multicomponent LMB₁ mammaglobin -- Corixa LMB 7 LMB 9 -- Battelle Memorial Institute, NIH mammastatin -- Biotherapeutics mannan-binding lectin -- Natlmmu LM-CD45 --- Cantab Pharmaceuticals mannan-MUC1 -- Psiron Iovastatin -- Merck MAP 30 LSA-3 Marinovir -- Phytera LT-ß receptor -- Biogen lung cancer vaccine -- Corixa MARstem -- Maret MB-015 -- Mochida lusupultide -- Scios MBP -- ImmuLogic L-Vax -- AVAX MCI-028 -- Mitsubishi-Tokyo LY 355455 -- Eli Lilly MCIF -- Human Genome Sciences LY 366405 -- Eli Lilly MDC --- Advanced BioScience -- Akzo LY-355101 -- Eli Lilly Lyme disease DNA vaccine -- Vical/Aventis Nobel, ICOS MDX 11 -- Medarex Pasteur MDX 210 -- Medarex MDX 22 -- Medarex

FIG. 1Q

MDX 22

Methionine lyase gene therapy --MDX 240 -- Medarex AntiCancer **MDX 33** Met-RANTES – Genexa Biomedical, MDX 44 -- Medarex MDX 447 -- Medarex Serono Metreleptin MDX H210 -- Medarex MDX RA -- Houston BioTech., Medarex MGDF -- Kirin MGV -- Progenics ME-104 -- Pharmexa micrin -- Endocrine Measles vaccine microplasmin -- ThromboGenics Mecasermin -- Cephalon/Chiron, Chiron MIF -- Genetics Institute MEDI 488 -- Medimmune migration inhibitory factor -- NIH MEDI 500 Mim CD4.1 – Xycte Therapies MEDI 507 -- BioTransplant mirostipen -- Human Genome Sciences melanin concentrating hormone ---MK 852 -- Merck Neurocrine Biosciences Mobenakin -- NIS melanocortins -- OMRF Melanoma monoclonal antibodies -- Viragenmolgramostim -- Genetics Institute, Novartis monoclonal antibodies -- Abgenix/Celltech, melanoma vaccine -- GlaxoSmithKline, Immusol/ Medarex, Viragen/ Roslin Akzo Nobel, Avant, Aventis Pasteur, Institute, Cambridge Antibody Tech./Elan Bavarian Nordic, Biovector, CancerVax, Genzyme Molecular Oncology, Humbolt, MAb 108 – ImClone Systems, Memorial, NYU, Oxxon MAb 10D5 --MAb 14.18-interleukin-2 immunocytokine --Melanoma vaccine Magevac -- Therion memory enhancers -- Scios Lexigen MAb 14G2a -meningococcal B vaccine -- Chiron MAb 15A10 meningococcal vaccine -- CAMR Meningococcal vaccine group B conjugate - MAb 170 -- Biomira - North American Vaccine MAb 177Lu CC49 ---MAb 17F9 Meningococcal vaccine group B MAb 1D7 recombinant -- BioChem Vaccines, MAb 1F7 - Immune Network Microscience Meningococcal vaccine group Y conjugate - MAb 1H10-doxorubicin conjugate MAb 26-2F North American Vaccine Meningococcal vaccine groups A B and C MAb 2A11 MAb 2E1 -- RW Johnson conjugate -- North American Vaccine MAb 2F5 Mepolizumab -- GlaxoSmithKline MAb 31.1 -- International BioImmune Metastatin – EntreMed, Takeda Met-CkB7 -- Human Genome Sciences MAb 32 -- Cambridge Antibody Tech., met-enkephalin -- TNI METH-1 -- Human Genome Sciences Peptech MAb 323A3 -- Centocor methioninase -- AntiCancer MAb 3C5

FIG. 1R

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MAb C242-PE conjugate MAb 3F12 MAb c30-6 MAb 3F8 MAb CA208-cytorhodin-S conjugate ---MAb 42/6 MAb 425 -- Merck KGaA Hoechst Japan MAb 447-52D -- Merck Sharp & Dohme MAb CC49 -- Enzon MAb 45-2D9- – haematoporphyrin MAb ch14.18 – MAb CH14.18-GM-CSF fusion protein -conjugate MAb 4B4 Lexigen MAb 4E3-CPA conjugate -- BCM Oncologia MAb chCE7 MAb 4E3-daunorubicin conjugate MAb CI-137 -- AMRAD MAb cisplatin conjugate MAb 50-6 MAb CLB-CD19 MAb 50-61A – Institut Pasteur MAb CLB-CD19v MAb 5A8 -- Biogen MAb 791T/36-methotrexate conjugate MAb CLL-1 -- Peregrine MAb CLL-1-GM-CSF conjugate MAb 7c11.e8 MAb CLL-1-IL-2 conjugate -- Peregrine MAb 7E11 C5-selenocystamine conjugate MAb CLN lgG -- doxorubicin conjugates MAb 93KA9 -- Novartis MAb A5B7-cisplatin conjugate --MAb conjugates - Tanox Biodynamics Research, Pharmacia MAb D612 MAb Dal B02 MAb A5B7-I-131 MAb DC101 -- ImClone MAb A7 MAb EA 1 – MAb A717 -- Exocell MAb A7-zinostatin conjugate MAb EC708 - Biovation MAb EP-5C7 -- Protein Design Labs MAb ABX-RB2 -- Abgenix MAb ERIC-1 -- ICRT MAb ACA 11 MAb F105 gene therapy MAb AFP-I-131 – Immunomedics MAb FC 2.15 MAb AP1 MAb G250 -- Centocor MAb AZ1 MAb B3-LysPE40 conjugate MAb GA6 MAb GA733 MAb B4 – United Biomedical MAb B43 Genistein-conjugate MAb Gliomab-H --- Viventia Biotech MAb B43.13-Tc-99m -- Biomira MAb HB2-saporin conjugate MAb B43-PAP conjugate MAb HD 37 – MAb B4G7-gelonin conjugate MAb HD37-ricin chain-A conjugate MAb HNK20 -- Acambis MAb BCM 43-daunorubicin conjugate --MAb huN901-DM1 conjugate --BCM Oncologia ImmunoGen MAb BIS-1 MAb BMS 181170 -- Bristol-Myers Squibb MAb I-131 CC49 -- Corixa MAb ICO25 MAb BR55-2 MAb ICR12-CPG2 conjugate MAb BW494 MAb C 242-DM1 conjugate -- ImmunoGen MAb ICR-62

FIG. 1S

MAb R-24 MAb IRac-ricin A conjugate MAb R-24 α Human GD3 -- Celltech MAb K1 MAb KS1-4-methotrexate conjugate MAb RFB4-ricin chain A conjugate MAb RFT5-ricin chain A conjugate MAb L6 -- Bristol-Myers Squibb, Oncogen MAb SC 1 MAb LiCO 16-88 MAb LL2-I-131 - Immunomedics MAb SM-3 -- ICRT MAb SMART 1D10 -- Protein Design Labs MAb LL2-Y-90 MAb SMART ABL 364 -- Novartis MAb LS2D617 -- Hybritech MAb LYM-1-gelonin conjugate MAb SN6f MAb SN6f-deglycosylated ricin A chain MAb LYM-1-I-131 MAb LYM-1-Y-90 conjugate -MAb SN6i MAb LYM-2 -- Peregrine MAb SN7-ricin chain A conjugate MAb M195 MAb T101-Y-90 conjugate -- Hybritech MAb M195-bismuth 213 conjugate --MAb T-88 -- Chiron Protein Design Labs MAb M195-gelonin conjugate MAb TB94 -- Cancer ImmunoBiology MAb TEC 11 MAb M195-I-131 MAb TES-23 -- Chugai MAb M195-Y-90 MAb TM31 -- Avant MAb MA 33H1 -- Sanofi MAb TNT-1 -- Cambridge Antibody Tech., MAb MAD11 Peregrine MAb MGb2 MAb TNT-3 MAb MINT5 MAb TNT-3 -- IL2 fusion protein -.MAb MK2-23 MAb MOC31 ETA(252-613) conjugate MAb TP3-At-211 MAb TP3-PAP conjugate --MAb MOC-31-In-111 MAb UJ13A -- ICRT MAb MOC-31-PE conjugate MAb UN3 MAb MR6 – MAb ZME-018-gelonin conjugate MAb MRK-16 -- Aventis Pasteur MAb-BC2 -- GlaxoSmithKline MAb MS11G6 MAb-DM1 conjugate -- ImmunoGen MAb MX-DTPA BrE-3 MAb-ricin-chain-A conjugate -- XOMA MAb MY9 MAb-temoporfin conjugates MAb Nd2 -- Tosoh Monopharm C -- Viventia Biotech MAb NG-1 -- Hygeia monteplase -- Eisai MAb NM01 – Nissin Food montirelin hydrate -- Gruenenthal MAb OC 125 moroctocog alfa -- Genetics Institute MAb OC 125-CMA conjugate Moroctocog-alfa -- Pharmacia MAb OKI-1 -- Ortho-McNeil MP 4 MAb OX52 -- Bioproducts for Science MP-121 -- Biopharm MAb PMA5 MP-52 -- Biopharm MAb PR1 MRA -- Chugai MAb prost 30 FIG. 1T

Neuroprotective vaccine -- University of MS 28168 -- Mitsui Chemicals, Nihon Auckland Schering MSH fusion toxin -- Ligand neurotrophic chimaeras -- Regeneron neurotrophic factor - NsGene, CereMedix MSI-99 -- Genaera NeuroVax -- Immune Response MT 201 -- Micromet neurturin -- Genentech Muc-1 vaccine -- Corixa neutral endopeptidase -- Genentech mucosal tolerance - Aberdeen NGF enhancers -- NeuroSearch mullerian inhibiting subst muplestim -- Genetics Institute, Novartis, NHL vaccine -- Large Scale Biology NIP45 -- Boston Life Sciences **DSM Anti-Infectives** NKI-B20 murine MAb - KS Biomedix Mutant somatropin -- JCR Pharmaceutical NM 01 - Nissin Food NMI-139 -- NitroMed MV 833 -- Toagosei NMMP -- Genetics Institute Mycoplasma pulmonis vaccine NN-2211 -- Novo Nordisk Mycoprex -- XOMA Noggin -- Regeneron myeloperoxidase -- Henogen myostatin -- Genetics Institute Nonacog alfa Norelin -- Biostar Nacolomab tafenatox -- Pharmacia nagrestipen - British Biotech Norwalk virus vaccine NRLU 10 -- NeoRx NAP-5 - Corvas Intl. NRLU 10 PE -- NeoRx NAPc2 - Corvas Intl. NT-3 -- Regeneron nartograstim -- Kyowa Natalizumab -- Protein Design Labs NT-4/5 -- Genentech NU 3056 Nateplase - NIH, Nihon Schering NU 3076 nateplase -- Schering AG NX 1838 -- Gilead Sciences NBI-3001 - Neurocrine Biosci. NY ESO-1/CAG-3 antigen -- NIH NBI-5788 -- Neurocrine Biosci. NYVAC-7 -- Aventis Pasteur NBI-6024 -- Neurocrine Biosci. NZ-1002 -- Novazyme Nef inhibitors -- BRI Neisseria gonorrhoea vaccine -- Antex obesity therapy -- Nobex OC 10426 -- Ontogen Biologics OC 144093 -- Ontogen Neomycin B-arginine conjugate Nerelimomab -- Chiron OCIF -- Sankyo Oct-43 -- Otsuka Nerve growth factor – Amgen – Chiron, OK PSA - liposomal Genentech OKT3-gamma-1-ala-ala Nerve growth factor gene therapy OM 991 nesiritide citrate -- Scios OM 992 neuregulin-2 -- CeNeS Omalizumab -- Genentech neurocan -- NYU neuronal delivery system -- CAMR oncoimmunin-L -- NIH Oncolysin B -- ImmunoGen

FIG. 1U

PAM 4 -- Merck Oncolysin CD6 -- ImmunoGen pamiteplase -- Yamanouchi Oncolysin M -- ImmunoGen pancreatin, Minitabs -- Eurand Oncolysin S -- ImmunoGen Pangen -- Fournier Oncophage -- Antigenics Pantarin - Selective Genetics Oncostatin M -- Bristol-Myers Squibb Parainfluenza virus vaccine – Pharmacia, OncoVax-CL -- Jenner Biotherapies Pierre Fabre OncoVax-P -- Jenner Biotherapies onercept -- Yeda paraoxanase -- Esperion parathyroid hormone - Abiogen, Korea onychomycosis vaccine -- Boehringer Green Cross Ingelheim Parathyroid hormone (1-34) -opebecan -- XOMA Chugai/Suntory opioids -- Arizona Parkinson's disease gene therapy -- Cell Opreivekin -- Genetics Institute Genesys/ Ceregene Org-33408 b-- Akzo Nobel Parvovirus vaccine -- MedImmune Orolip DP -- EpiCept PCP-Scan - Immunomedics oryzacystatin OSA peptides – GenSci Regeneration PDGF cocktail -- Theratechnologies peanut allergy therapy -- Dynavax osteoblast-cadherin GF -- Pharis Osteocalcin-thymidine kinase gene therapy PEG anti-ICAM MAb -- Boehringer Ingelheim osteogenic protein -- Curis osteopontin - OraPharma PEG asparaginase -- Enzon PEG glucocerebrosidase osteoporosis peptides - Integra, Telios osteoprotegerin - Amgen, SnowBrand PEG hirudin – Knoll otitis media vaccines -- Antex Biologics PEG interferon-alpha-2a -- Roche PEG interferon-alpha-2b + ribavirin ovarian cancer -- University of Alabama OX40-IgG fusion protein -- Cantab, Xenova Biogen, Enzon, ICN Pharmaceuticals, Schering-Plough P 246 -- Diatide PEG MAb A5B7 -P 30 -- Alfacell Pegacaristim – Amgen -- Kirin Brewery -p1025 -- Active Biotech P-113[^] -- Demegen ZymoGenetics P-16 peptide -- Transition Therapeutics Pegaldesleukin -- Research Corp pegaspargase -- Enzon p43 -- Ramot pegfilgrastim -- Amgen P-50 peptide -- Transition Therapeutics PEG-interferon Alpha -- Viragen p53 + RAS vaccine -- NIH, NC! PEG-interferon Alpha 2A -- Hoffman La-PACAP(1-27) analogue Roche paediatric vaccines -- Chiron PEG-interferon Alpha 2B -- Schering-Pafase -- ICOS PAGE-4 plasmid DNA -- IDEC Plough PEG-r-hirudin -- Abbott PAI-2 -- Biotech Australia, Human PEG-uricase -- Mountain View Therapeutics Pegvisomant – Genentech Palivizumab -- Medimmune

FIG. 1V

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PEGylated proteins, PolyMASC -- Valentis Pharmaprojects No. 5947 -- StressGen PEGylated recombinant native human leptin Pharmaprojects No. 5961 -Theratechnologies -- Roche Pharmaprojects No. 5962 -- NIH Pemtumomab Pharmaprojects No. 5966 -- NIH Penetratin -- Cyclacel Pharmaprojects No. 5994 -- Pharming Pepscan - Antisoma Pharmaprojects No. 5995 -- Pharming peptide G - Peptech, ICRT Pharmaprojects No. 6023 -- IMMUCON peptide vaccine -- NIH ,NCl Pharmaprojects No. 6063 -- Cytoclonal Pexelizumab Pharmaprojects No. 6073 -- SIDDCO pexiganan acetate -- Genaera Pharmaprojects No. 6115 -- Genzyme Pharmaprojects No. 3179 -- NYU Pharmaprojects No. 3390 -- Ernest Orlando Pharmaprojects No. 6227 -- NIH Pharmaprojects No. 3417 -- Sumitomo Pharmaprojects No. 6230 -- NIH Pharmaprojects No. 3777 -- Acambis Pharmaprojects No. 6236 -- NIH Pharmaprojects No. 4209 -- XOMA Pharmaprojects No. 6243 -- NIH Pharmaprojects No. 4349 – Baxter Intl. Pharmaprojects No. 6244 -- NIH Pharmaprojects No. 6281 -- Senetek Pharmaprojects No. 4651 Pharmaprojects No. 4915 -- Avanir Pharmaprojects No. 6365 -- NIH Pharmaprojects No. 5156 -- Rhizogenics Pharmaprojects No. 6368 -- NIH Pharmaprojects No. 6373 -- NIH Pharmaprojects No. 5200 -- Pfizer Pharmaprojects No. 6408 - Pan Pacific Pharmaprojects No. 5215 -- Origene Pharmaprojects No. 6410 -- Athersys Pharmaprojects No. 5216 -- Origene Pharmaprojects No. 6421 – Oxford Pharmaprojects No. 5218 -- Origene Pharmaprojects No. 5267 -- ML **GlycoSciences** Pharmaprojects No. 6522 -- Maxygen Laboratories Pharmaprojects No. 6523 -- Pharis Pharmaprojects No. 5373 -- MorphoSys Pharmaprojects No. 5493 -- Metabolex Pharmaprojects No. 6538 -- Maxygen Pharmaprojects No. 6554 -- APALEXO Pharmaprojects No. 5707 -- Genentech Pharmaprojects No. 6560 -- Ardana Pharmaprojects No. 5728 -- Autogen Pharmaprojects No. 5733 -- BioMarin Pharmaprojects No. 6562 -- Bayer Pharmaprojects No. 5757 -- NIH Pharmaprojects No. 6569 -- Eos Phenoxazine Pharmaprojects No. 5765 - Gryphon Pharmaprojects No. 5830 -- AntiCancer Phenylase -- Ibex Pharmaprojects No. 5839 -- Dyax Pigment epithelium derived factor plasminogen activator inhibitor-1, Pharmaprojects No. 5849 -- Johnson & recombinant -- DuPont Pharmaceuticals Johnson Pharmaprojects No. 5860 -- Mitsubishi-Tokyo Pharmaprojects No. 5869 - Oxford

GlycoSciences |

Pharmaprojects No. 5883 -- Asahi Brewery

FIG. 1W

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prostate-specific antigen -- EntreMed Plasminogen activators -- Abbott Laboratories, American Home Products, protein A -- RepliGen Boehringer Mannheim, Chiron protein adhesives -- Enzon Corporation, DuPont Pharmaceuticals, Eli protein C - Baxter Intl., PPL Therapeutics, ZymoGenetics Lilly, Shionogi, Genentech, Genetics protein C activator - Gilead Sciences Institute, GlaxoSmithKline, Hemispherx Biopharma, Merck & Co, Novartis, protein kinase R antags -- NIH Pharmacia Corporation, Wakamoto, Yeda protirelin -- Takeda plasminogen-related peptides -- Bio-Tech. protocadherin 2 -- Caprion Pro-urokinase - Abbott, Bristol-Myers General/MGH Squibb, Dainippon, Tosoh -- Welfide platelet factor 4 -- RepliGen P-selectin glycoprotein ligand-1 -- Genetics Platelet-derived growth factor - Amgen --Institute **ZymoGenetics** pseudomonal infections -- InterMune plusonermin-- Hayashibara Pseudomonas vaccine -- Cytovax PMD-2850 -- Protherics PSGL-Ig -- American Home Products Pneumococcal vaccine -- Antex Biologics, PSP-94 -- Procyon Aventis Pasteur Pneumococcal vaccine intranasal --PTH 1-34 -- Nobex Quilimmune-M -- Antigenics BioChem Vaccines/Biovector R 101933 PR1A3 R 125224 -- Sankyo PR-39 RA therapy -- Cardion pralmorelin -- Kaken Rabies vaccine recombinant -- Aventis Pretarget-Lymphoma -- NeoRx Pasteur, BioChem Vaccines, Kaketsuken Priliximab -- Centocor **Pharmaceuticals** PRO 140 -- Progenics RadioTheraCIM -- YM BioSciences PRO 2000 -- Procept Ramot project No. 1315 -- Ramot PRO 367 -- Progenics Ramot project No. K-734A -- Ramot PRO 542 -- Progenics Ramot project No. K-734B -- Ramot pro-Apo A-1 -- Esperion RANK -- Immunex prolactin -- Genzyme Prosaptide TX14(A) -- Bio-Tech. General ranpirnase -- Alfacell ranpirnase-anti-CD22 MAb -- Alfacell prostate cancer antbodies – Immunex, RANTES inhibitor -- Milan UroCor RAPID drug delivery systems -- ARIAD prostate cancer antibody therapy -rasburicase -- Sanofi Genentech/UroGenesys, rBPI-21, topical -- XOMA Genotherapeutics prostate cancer immunotherapeutics -- The RC 529 -- Corixa rCFTR -- Genzyme Transgenics PSMA Development Company prostate cancer vaccine -- Aventis Pasteur, RD 62198 rDnase -- Genentech Zonagen, Corixa, Dendreon, Jenner RDP-58 -- SangStat Biotherapies, Therion Biologics

FIG. 1X

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Ribozyme gene therapy -- Genset RecepTox-Fce -- Keryx Rickettsial vaccine recombinant RecepTox-GnRH - Keryx, MTR RIGScan CR -- Neoprobe **Technologies** RIP-3 -- Rigel RecepTox-MBP – Keryx, MTR RK-0202 -- RxKinetix Technologies RLT peptide -- Esperion recFSH -- Akzo Nobel, Organon rM/NEI -- IVAX REGA 3G12 rmCRP -- Immtech Regavirumab -- Teijin RN-1001 -- Renovo relaxin -- Connetics, Corp RN-3 -- Renovo Renal cancer vaccine -- Macropharm RNAse conjugate -- Immunomedics repifermin -- Human Genome Sciences Respiratory syncytial virus PFP-2 vaccine -- RO 631908 -- Roche Rotavirus vaccine -- Merck Wyeth-Lederle Respiratory syncytial virus vaccine -RP 431 -- DuPont Pharmaceuticals GlaxoSmithKline, Pharmacia, Pierre Fabre RP-128 -- Resolution Respiratory syncytial virus vaccine RPE65 gene therapy – RPR 110173 -- Aventis Pasteur inactivated RPR 115135 -- Aventis Pasteur Respiratory syncytial virus-parainfluenza RPR 116258A -- Aventis Pasteur virus vaccine -- Aventis Pasteur, rPSGL-Ig -- American Home Products Pharmacia r-SPC surfactant -- Byk Gulden Reteplase -- Boehringer Mannheim, rV-HER-2/neu -- Therion Biologics Hoffman La-Roche SA 1042 -- Sankyo Retropep -- Retroscreen sacrosidase - Orphan Medical RFB4 (dsFv) PE38 Sant 7 RFI 641 -- American Home Products Sargramostim -- Immunex RFTS -- UAB Research Foundation RG 12986 -- Aventis Pasteur saruplase -- Gruenenthal Satumomab -- Cytogen RG 83852 -- Aventis Pasteur SB 1 -- COR Therapeutics RG-1059 -- RepliGen SB 207448 -- GlaxoSmithKline rGCR -- NIH SB 208651 -- GlaxoSmithKline rGLP-1 -- Restoragen SB 240683 -- GlaxoSmithKline rGRF -- Restoragen SB 249415 -- GlaxoSmithKline rh Insulin – Eli Lilly RHAMM targeting peptides -- Cangene SB 249417 -- GlaxoSmithKline rHb1.1 - Baxter Intl. SB 6 -- COR Therapeutics SB RA 31012 rhCC10 -- Claragen SC 56929 -- Pharmacia rhCG -- Serono SCA binding proteins - Curis, Enzon Rheumatoid arthritis gene therapy scFv(14E1)-ETA Berlex Laboratories, Rheumatoid arthritis vaccine -- Veterans Schering AG Affairs Medical Center ScFv(FRP5)-ETA rhLH -- Serono

FIG. 1Y

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somatomedin-1 - GroPep, Mitsubishi-ScFv6C6-PE40 -SCH 55700 -- Celltech Tokyo, NIH somatomedin-1 carrier protein -- Insmed Schistosomiasis vaccine -- Glaxo somatostatin -- Ferring Wellcome/Medeva, Brazil SCPF -- Advanced Tissue Sciences Somatotropin/ Human Growth Hormone -- Bio-Tech. scuPA-suPAR complex -- Hadasit General, Eli Lilly SD-9427 -- Pharmacia somatropin -- Bio-Tech. General, Alkermes, SDF-1 -- Ono ProLease, Aventis Behring, Biovector, SDZ 215918 -- Novartis Cangene, Dong-A, Eli Lilly, Emisphere, SDZ 280125 -- Novartis Enact, Genentech, Genzyme Transgenics, SDZ 89104 -- Novartis Grandis/InfiMed, CSL, InfiMed, MacroMed, SDZ ABL 364 -- Novartis Novartis, Novo Nordisk, Pharmacia SDZ MMA 383 -- Novartis serine protease inhibs -- Pharis Serono, TranXenoGen somatropin derivative -- Schering AG sermorelin acetate -- Serono somatropin, AIR -- Eli Lilly SERP-1 -- Viron Somatropin, inhaled -- Eli Lilly/Alkermes sertenef -- Dainippon somatropin, Kabi -- Pharmacia serum albumin, Recombinant human -somatropin, Orasome -- Novo Nordisk Aventis Behring serum-derived factor -- Hadasit Sonermin -- Dainippon Pharmaceutical SP(V5.2)C -- Supertek Sevirumab -- Novartis SPf66 SGN 14 -- Seatle Genetics sphingomyelinase -- Genzyme SGN 15 -- Seatle Genetics SR 29001 -- Sanofi SGN 17/19 -- Seatle Genetics SR 41476 -- Sanofi SGN 30 -- Seatle Genetics SGN-10 -- Seatle Genetics SR-29001 -- Sanofi SS1(dsFV)-PE38 -- NeoPharm SGN-11 -- Seatle Genetics ß2 microglobulin -- Avidex SH 306 -- DuPont Pharmaceuticals ß2-microglobulin fusion proteins -- NIH Shanvac-B -- Shantha Shigella flexneri vaccine -- Avant, Acambis, ß-amyloid peptides -- CeNeS ß-defensin -- Pharis Novavax Staphylococcus aureus infections --Shigella sonnei vaccine – Inhibitex/ZLB sICAM-1 -- Boehringer Ingelheim Staphylococcus aureus vaccine conjugate --Silteplase -- Genzyme SIV vaccine -- Endocon, Institut Pasteur Nabi SK 896 -- Sanwa Kagaku Kenkyusho Staphylococcus therapy -- Tripep SK-827 -- Sanwa Kagaku Kenkyusho Staphylokinase – Biovation, Prothera, Skeletex -- CellFactors Thrombogenetics Streptococcal A vaccine -- M6 SKF 106160 -- GlaxoSmithKline Pharmaceuticals, North American Vaccine S-nitroso-AR545C --Streptococcal B vaccine -- Microscience SNTP -- Active Biotech

FIG. 1Z

TFPI -- EntreMed Streptococcal B vaccine recombinant -tgD-IL-2 -- Takeda Biochem Vaccines TGF-Alpha -- ZymoGenetics Streptococcus pyogenes vaccine TGF-ß -- Kolon STRL-33 -- NIH TGF-ß2 -- Insmed Subalin -- SRC VB VECTOR TGF-ß3 -- OSI SUIS -- United Biomedical Thalassaemia gene therapy -- Crucell SUIS-LHRH -- United Biomedical TheraCIM-h-R3 -- Center of Molecular SUN-E3001 -- Suntory Immunology, YM BioSciences super high affinity monoclonal antibodies --YM BioSciences Theradigm-HBV -- Epimmune Theradigm-HPV -- Epimmune Superoxide dismutase - Chiron, Enzon, Theradigm-malaria -- Epimmune Ube Industries, Bio-Tech, Yeda Theradigm-melanoma -- Epimmune superoxide dismutase-2 -- OXIS suppressin -- UAB Research Foundation TheraFab – Antisoma ThGRF 1-29 -- Theratechnologies SY-161-P5 -- ThromboGenics ThGRF 1-44 -- Theratechnologies SY-162 -- ThromboGenics thrombomodulin – Iowa, Novocastra Systemic lupus erythematosus vaccine --Thrombopoietin -- Dragon Pharmaceuticals, MedClone/VivoRx Genentech T cell receptor peptide vaccine thrombopoietin, Pliva --- Receptron T4N5 liposomes -- AGI Dermatics Thrombospondin 2 – TACI, soluble -- ZymoGenetics thrombostatin -- Thromgen targeted apoptosis -- Antisoma thymalfasin -- SciClone tasonermin -- Boehringer Ingelheim thymocartin - Gedeon Richter TASP thymosin Alpha1 -- NIH TASP-V thyroid stimulating hormone -- Genzyme Tat peptide analogues -- NIH tlCAM-1 -- Bayer TBP I -- Yeda Tick anticoagulant peptide -- Merck TBP || TIF -- Xoma TBV25H -- NIH Tc 99m ior cea1 -- Center of Molecular Tifacogin – Chiron, NIS, Pharmacia Tissue factor -- Genentech Immunology Tissue factor pathway inhibitor Tc 99m P 748 -- Diatide TJN-135 -- Tsumura Tc 99m votumumab -- Intracell Tc-99m rh-Annexin V - Theseus Imaging TM 27 -- Avant TM 29 -- Avant teceleukin -- Biogen TMC-151 – Tanabe Seiyaku tenecteplase -- Genentech TNF tumour necrosis factor -- Asahi Kasei Teriparatide -- Armour Pharmaceuticals, TNF Alpha -- Cytlmmune Asahi Kasei, Eli Lilly TNF antibody -- Johnson & Johnson terlipressin -- Ferring TNF binding protein -- Amgen testisin -- AMRAD TNF degradation product -- Oncotech Tetrafibricin -- Roche FIG. 1AA

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TNF receptor -- Immunex TNF receptor 1, soluble -- Amgen TNF Tumour necrosis factor-alpha -- Asahi Type I diabetes vaccine -- Research Corp Kasei, Genetech, Mochida TNF-Alpha inhibitor -- Tripep TNFR:Fc gene therapy - Targeted Genetics U 81749 -- Pharmacia TNF-SAM2 ToleriMab -- Innogenetics Toxoplasma gondii vaccine ---GlaxoSmithKline TP 9201 -- Telios TP10 -- Avant TP20 -- Avant tPA --- Centocor trafermin -- Scios TRAIL/Apo2L -- Immunex transferrin-binding proteins -- CAMR Transforming growth factor-beta-1 --Genentech transport protein -- Genesis TRH -- Ferring Triabin -- Schering AG Triconal Triflavin troponin I -- Boston Life Sciences TRP-2^ -- NIH trypsin inhibitor -- Mochida TSP-1 gene therapy --TT-232 TTS-CD2 -- Active Biotech Tuberculosis vaccine -- Aventis Pasteur, Genesis Tumor Targeted Superantigens -- Active Biotech -- Pharmacia tumour vaccines -- PhotoCure tumour-activated prodrug antibody conjugates -- Millennium/ImmunoGen tumstatin -- ILEX WP 652 Tuvirumab -- Novartis WT1 vaccine -- Corixa TV-4710 - Teva

TWEAK receptor -- Immunex

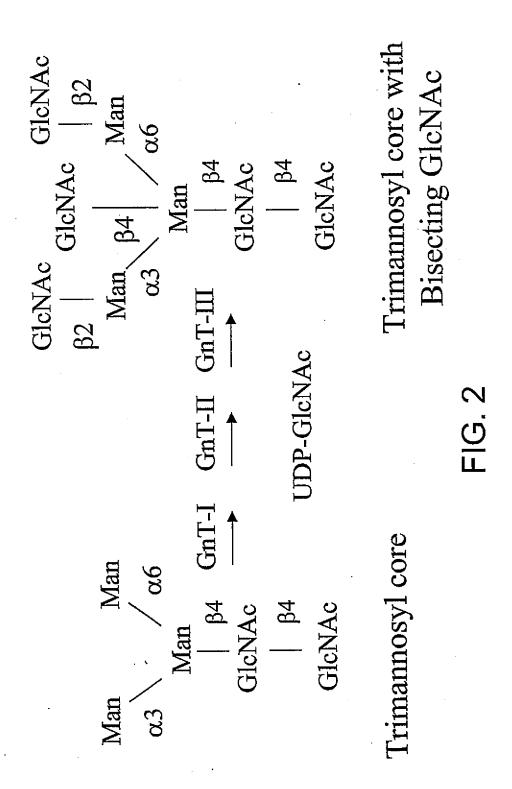
TXU-PAP TY-10721 - TOA Eiyo Typhoid vaccine CVD 908 U 143677 -- Pharmacia UA 1248 -- Arizona UGIF -- Sheffield UIC 2 UK 101 UK-279276 - Corvas Intl. urodilatin -- Pharis urofollitrophin -- Serono uteroferrin-- Pepgen V 20 -- GLYCODesign V2 vasopressin receptor gene therapy vaccines -- Active Biotech Varicella zoster glycoprotein vaccine --Research Corporation Technologies Varicella zoster virus vaccine live -- Cantab **Pharmaceuticals** Vascular endothelial growth factor – Genentech, University of California Vascular endothelial growth factors – R&D Systems vascular targeting agents -- Peregrine vasopermeation enhancement agents --Peregrine vasostatin -- NIH VCL -- Bio-Tech, General VEGF - Genentech, Scios VEGF inhibitor -- Chugai VEGF-2 -- Human Genome Sciences VEGF-Trap --- Regeneron viscumin, recombinant -- Madaus Vitaxin Vitrase -- ISTA Pharmaceuticals West Nile virus vaccine -- Bavarian Nordic

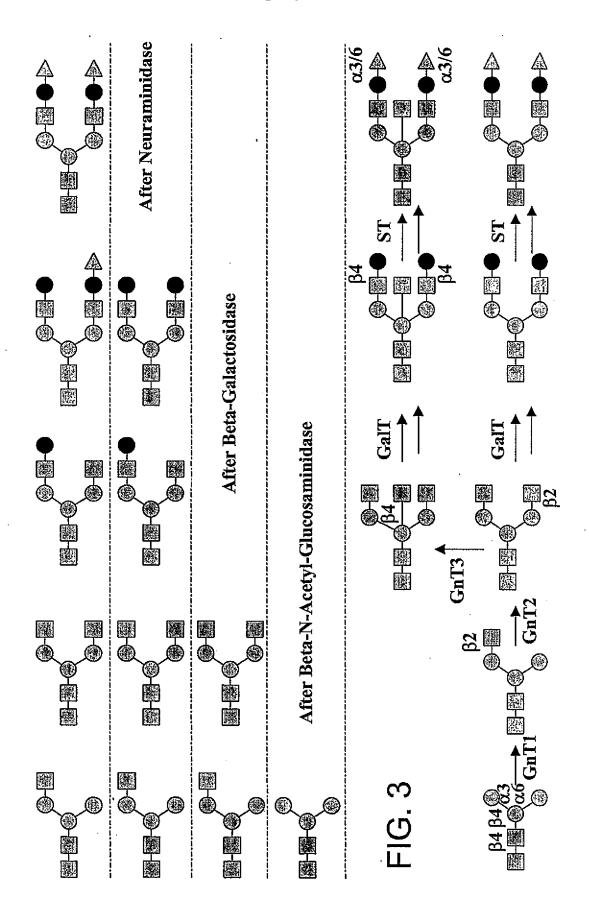
WX-293 -- Wilex BioTech. FIG. 1BB

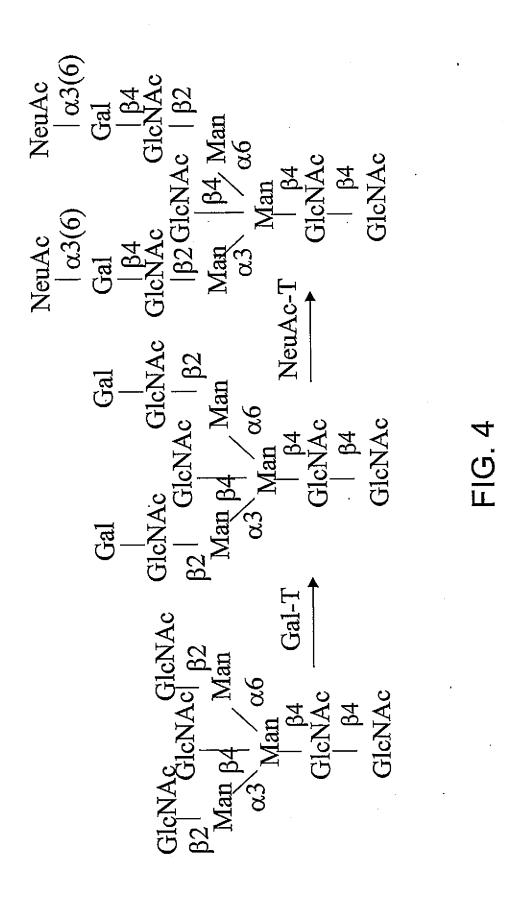
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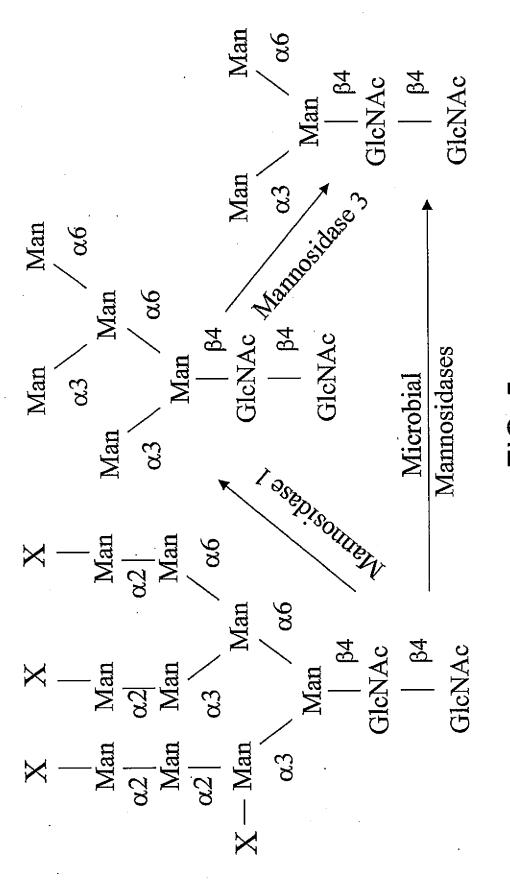
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WX-UK1 -- Wilex BioTech.
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XomaZyme-791 -- XOMA
XTL 001 -- XTL Biopharmaceuticals
XTL 002 -- XTL Biopharmaceuticals
yeast delivery system -- Globelmmune
Yersinia pestis vaccine
YIGSR-Stealth -- Johnson & Johnson
Yissum Project No. D-0460 -- Yissum

YM 207 -- Yamanouchi
YM 337 -- Protein Design Labs
Yttrium-90 labelled biotin
Yttrium-90-labeled anti-CEA MAb T84.66 -ZD 0490 -- AstraZeneca
ziconotide -- Elan
ZK 157138 -- Berlex Laboratories
Zolimomab aritox
Zorcell -- Immune Response
ZRXL peptides -- Novartis

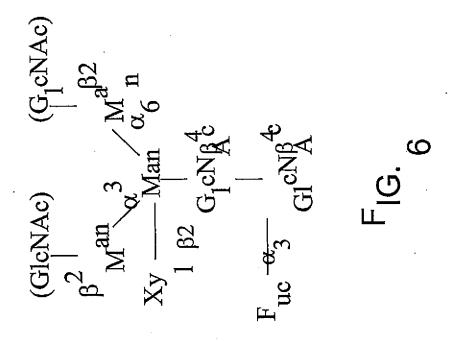




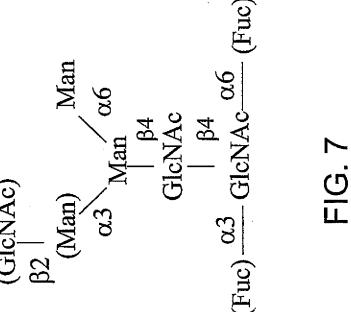


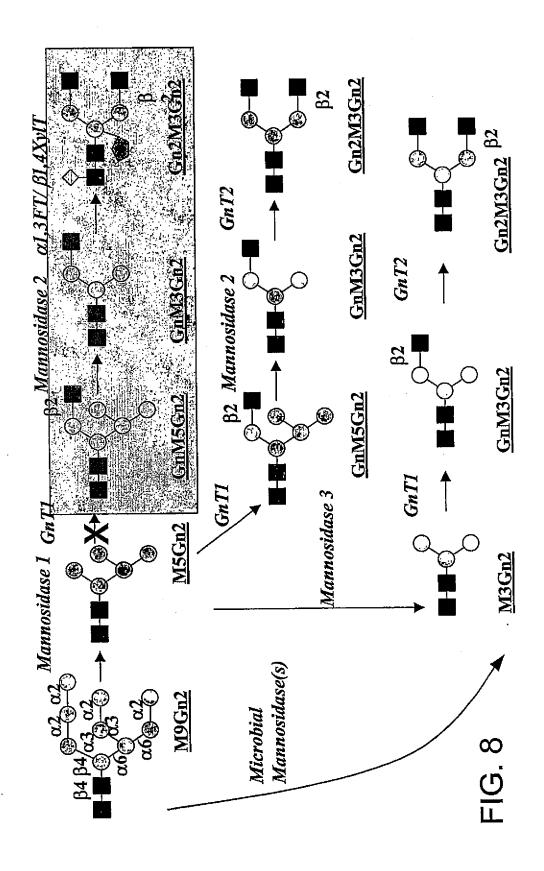


-16.5

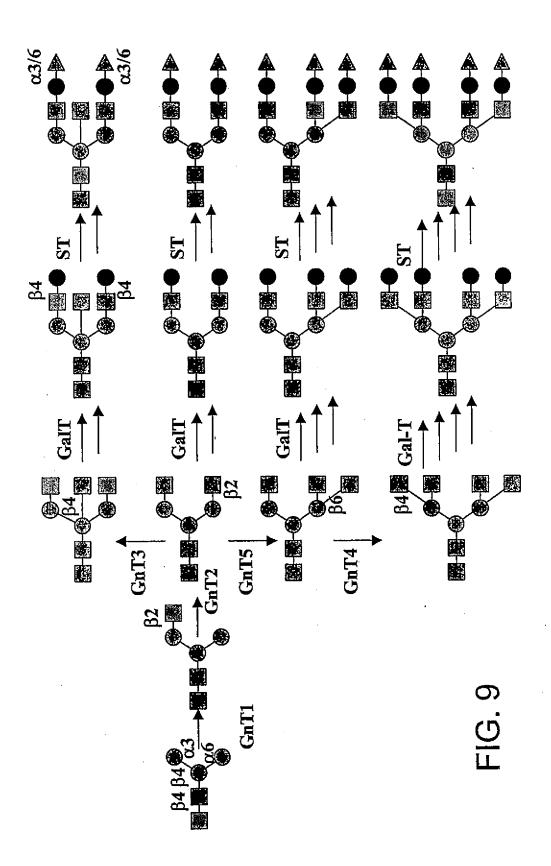


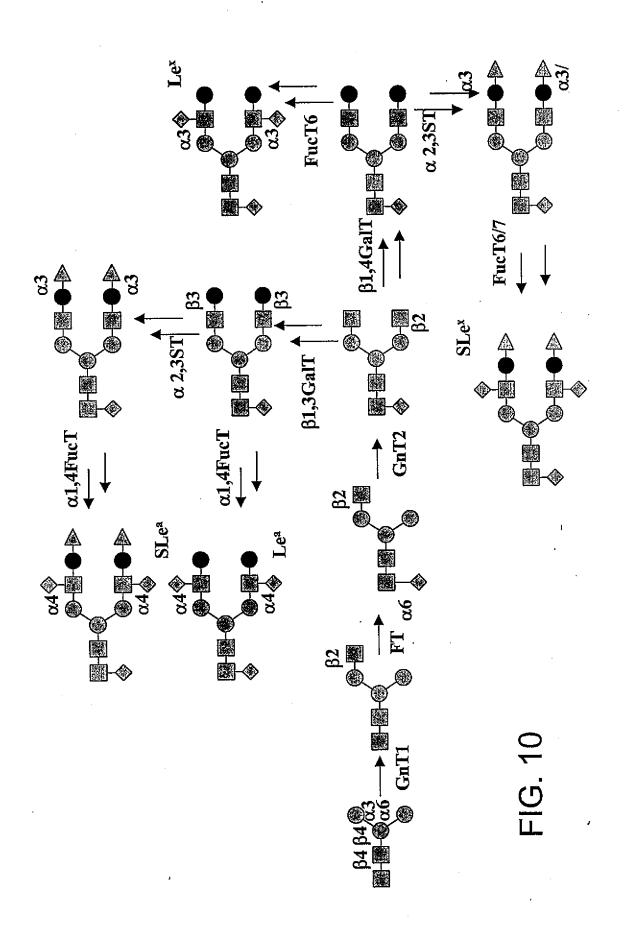
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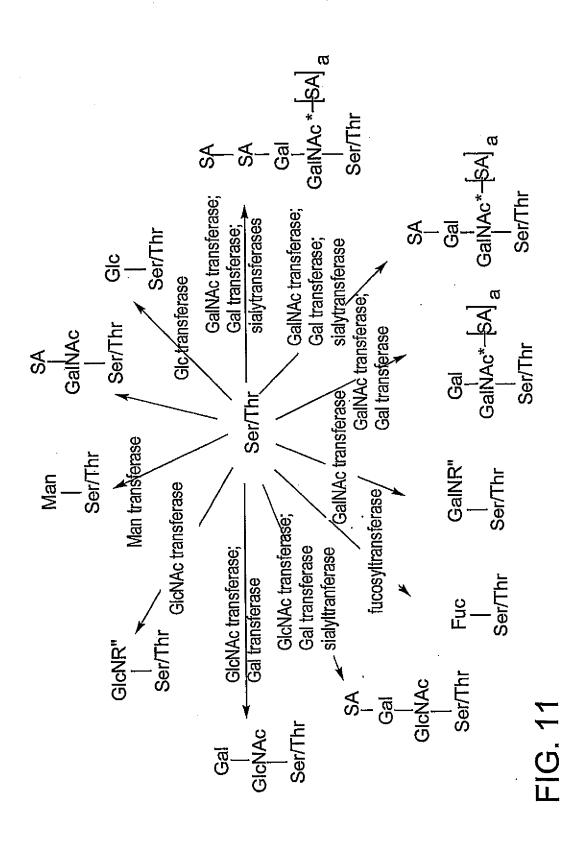




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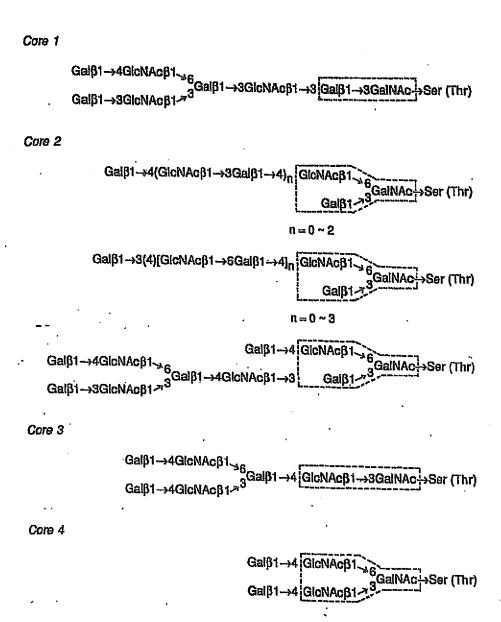
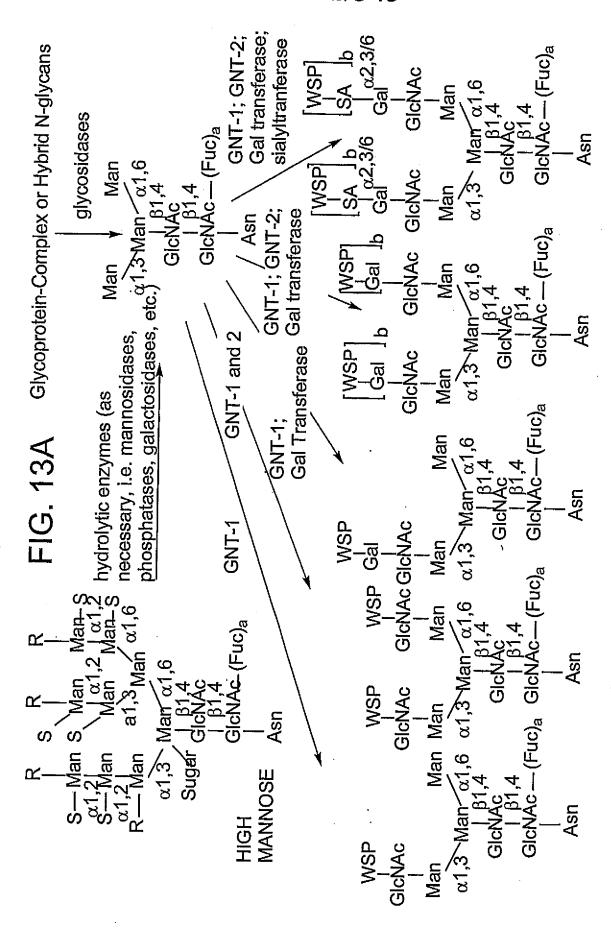
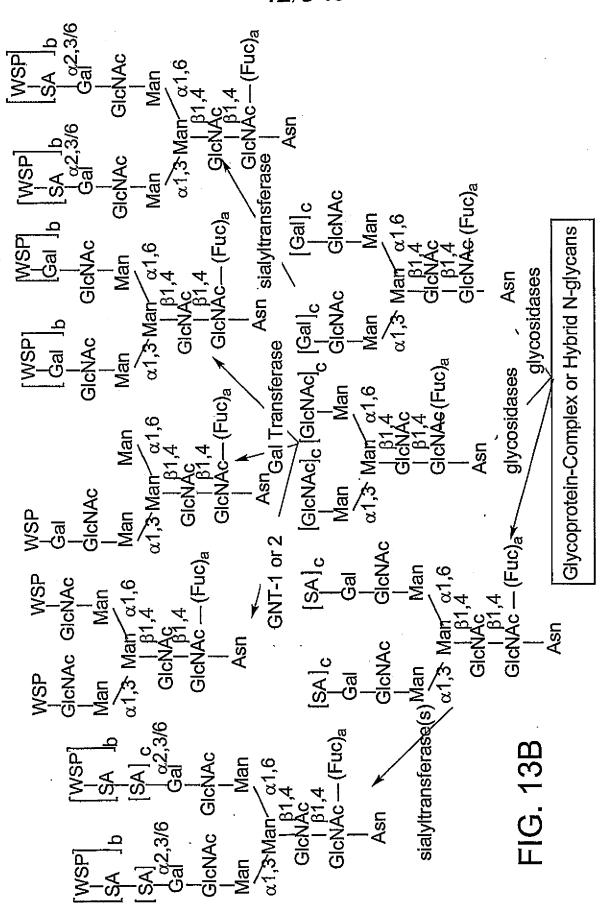


FIG. 12





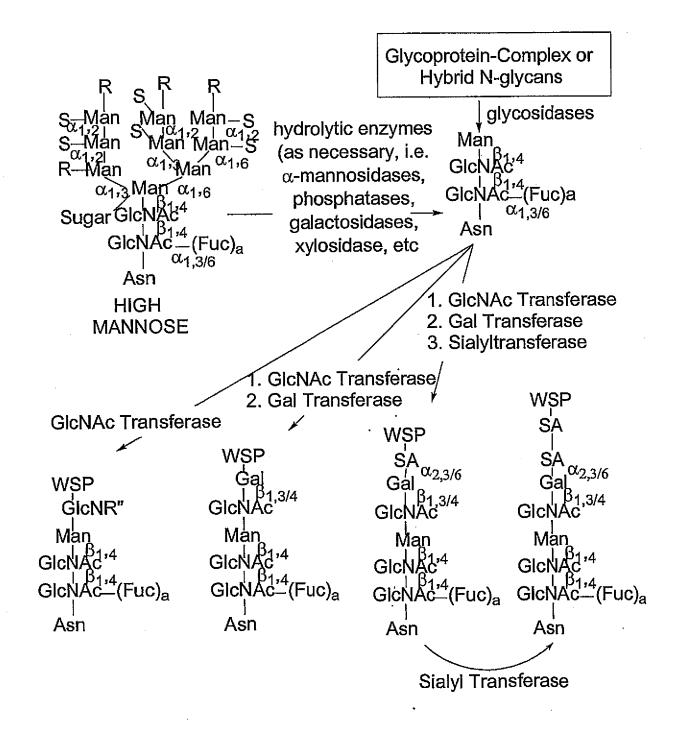


FIG. 14

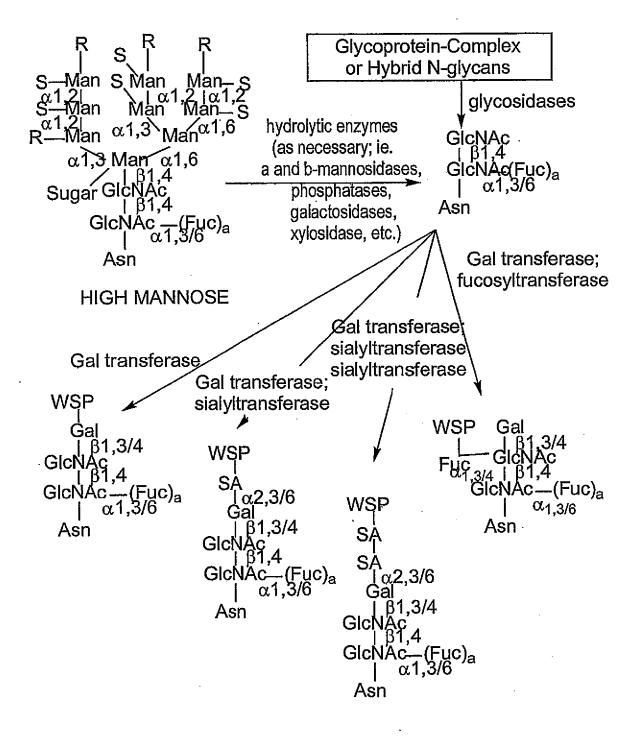


FIG. 15

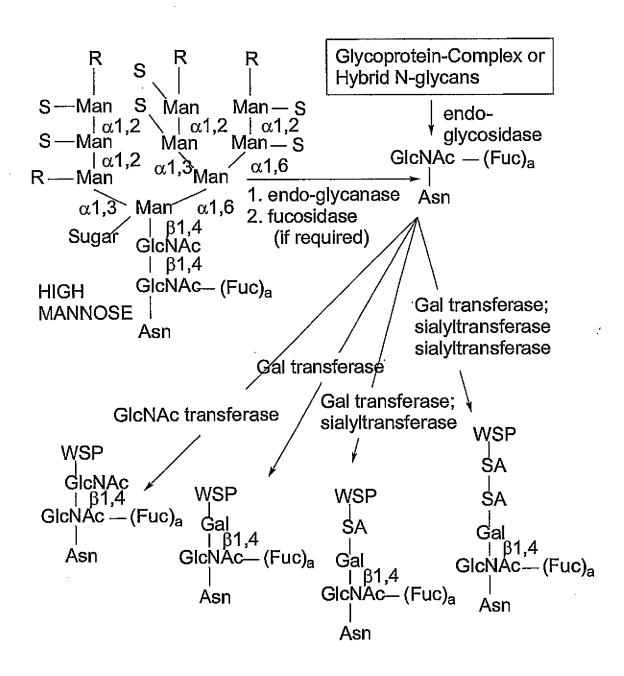
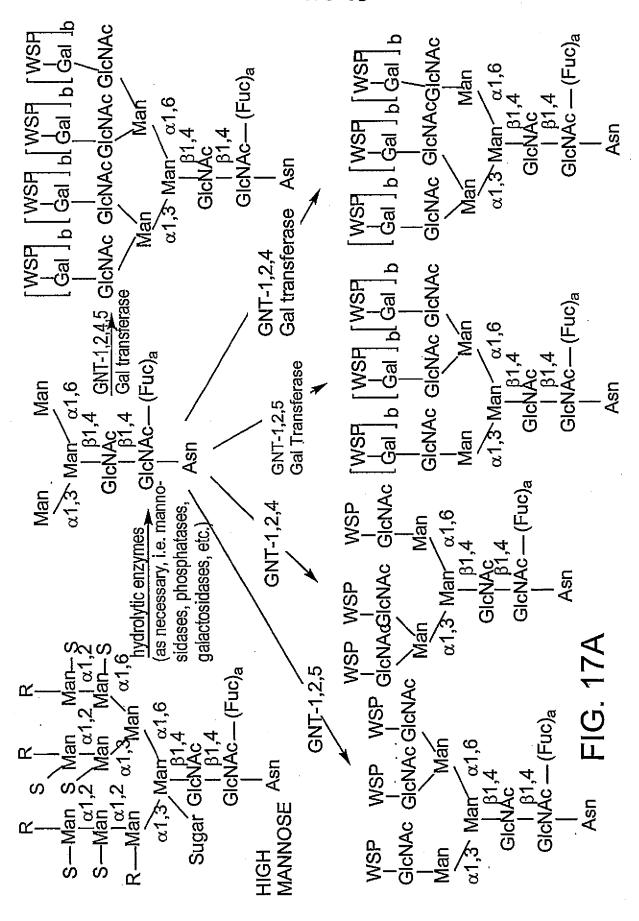
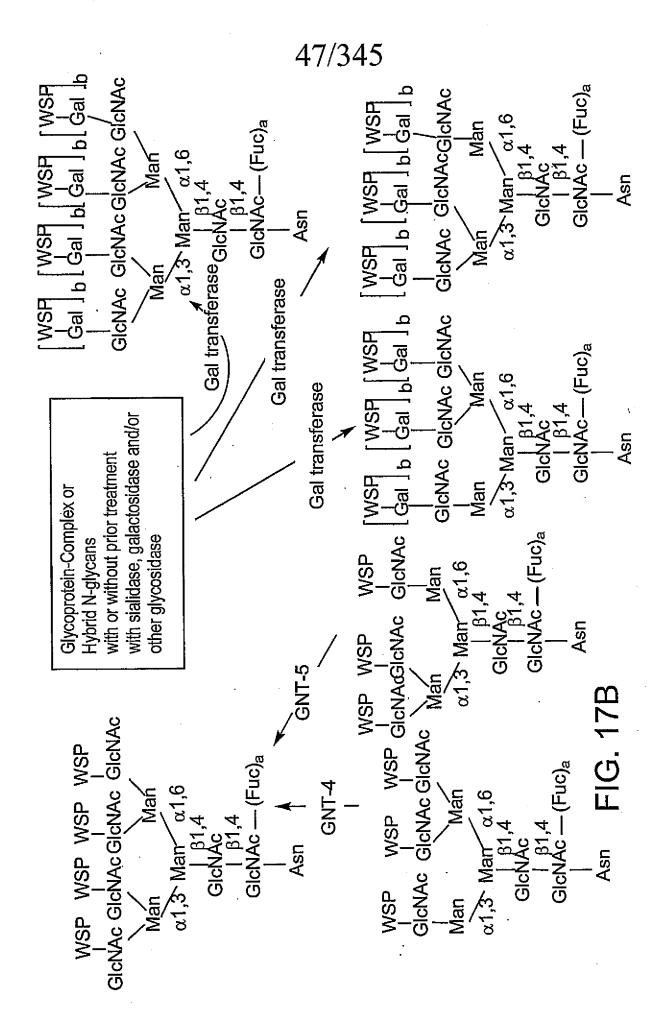
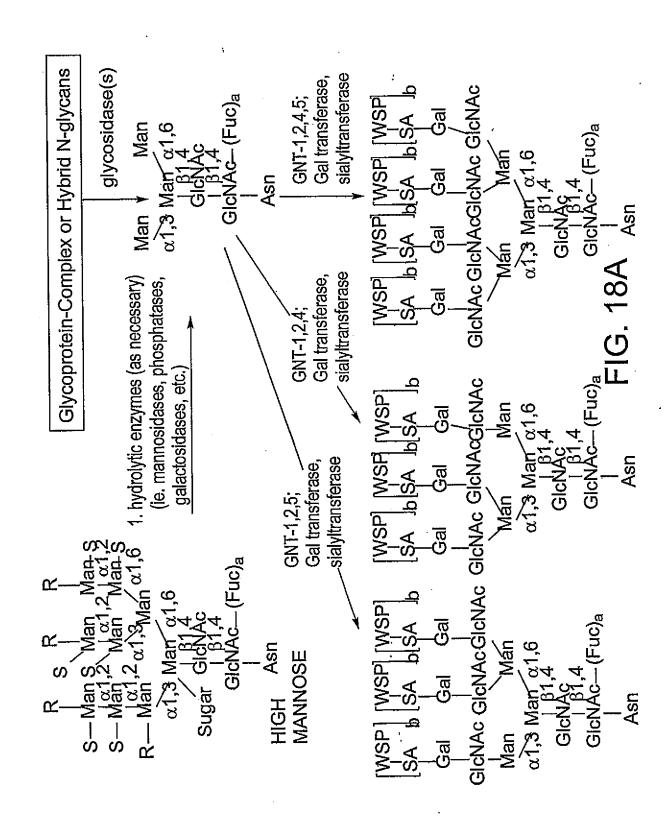


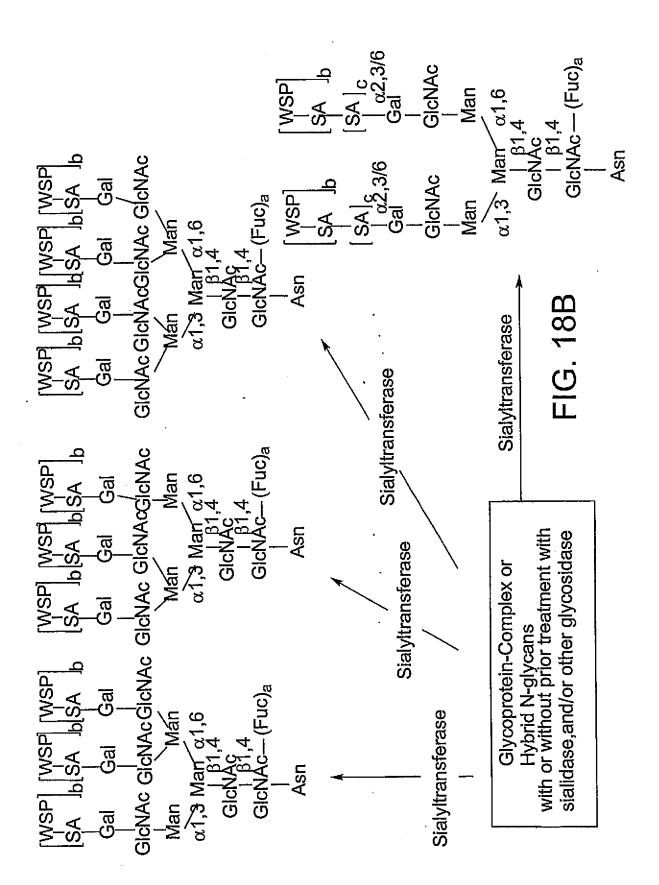
FIG. 16



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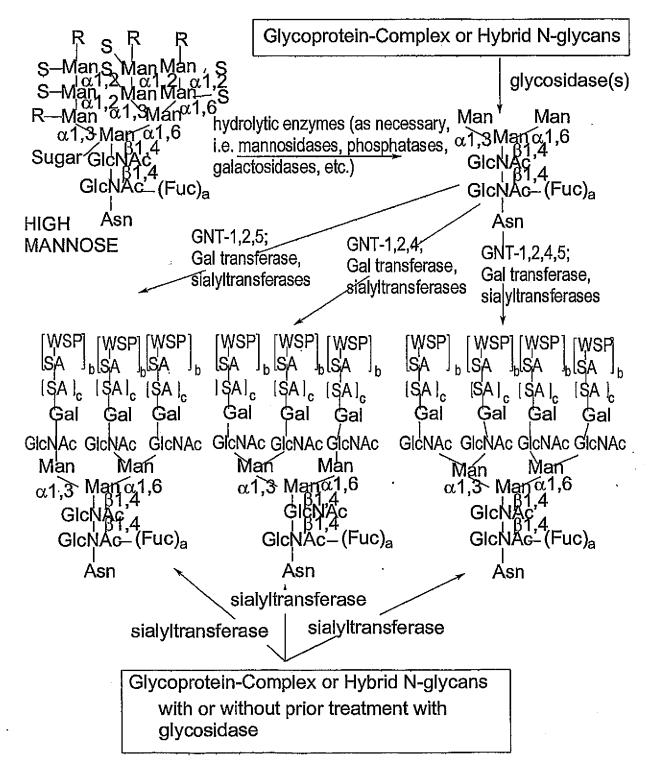
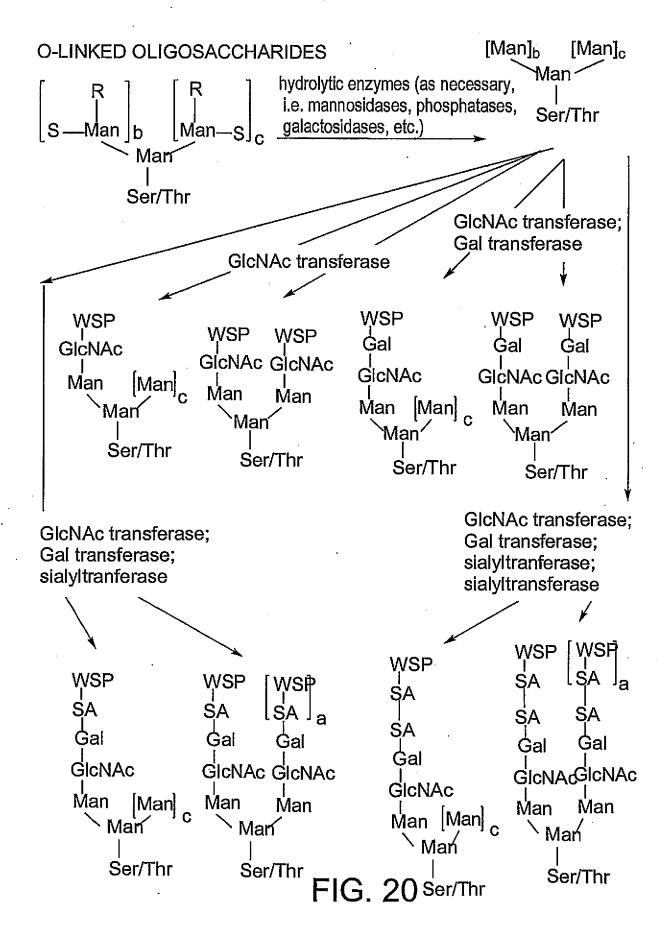
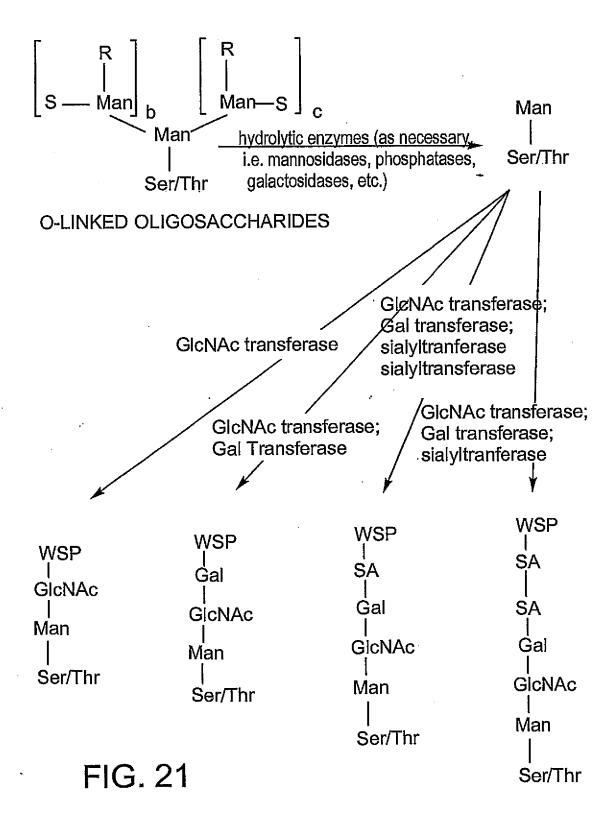


FIG. 19





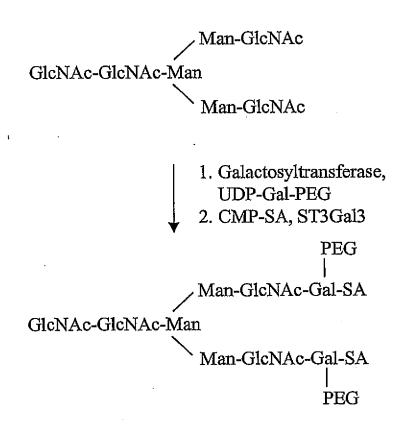


FIG. 22A

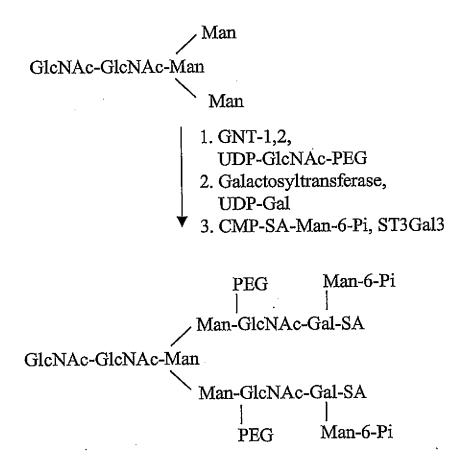
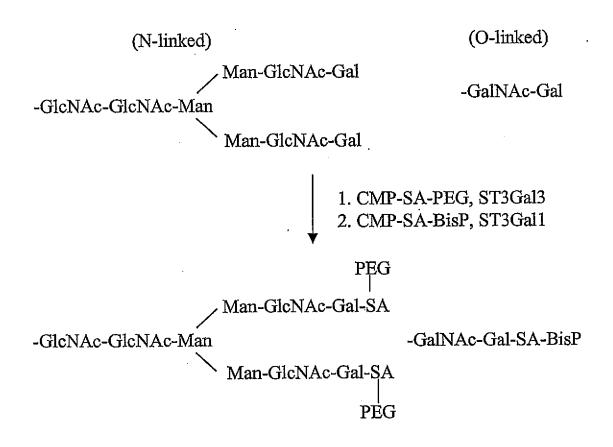


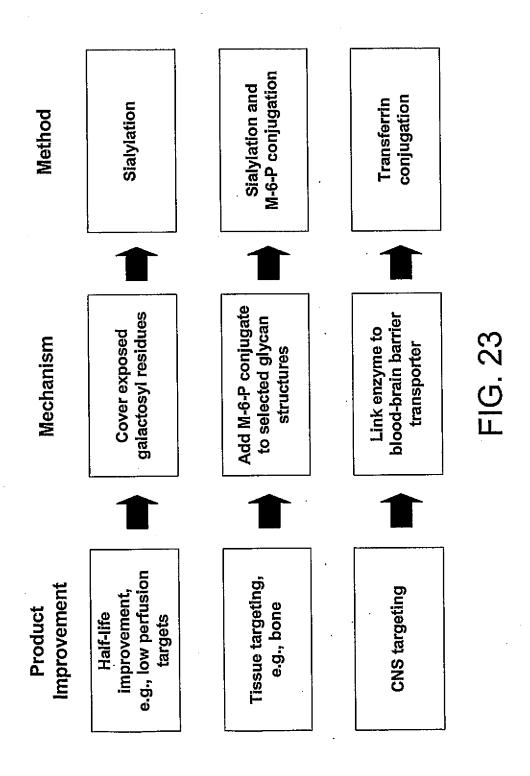
FIG. 22B



BisP =Linker-HN-CH(PO₃)₂

FIG. 22C

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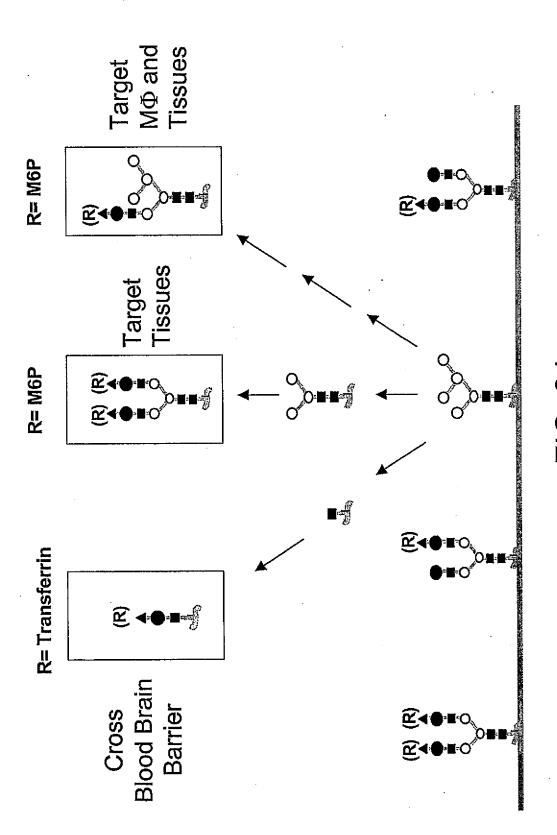
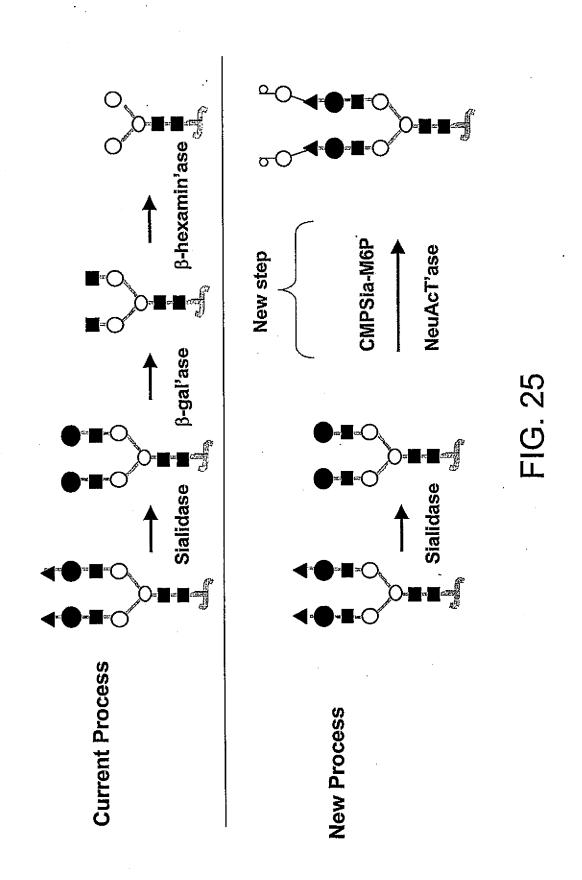


FIG. 24

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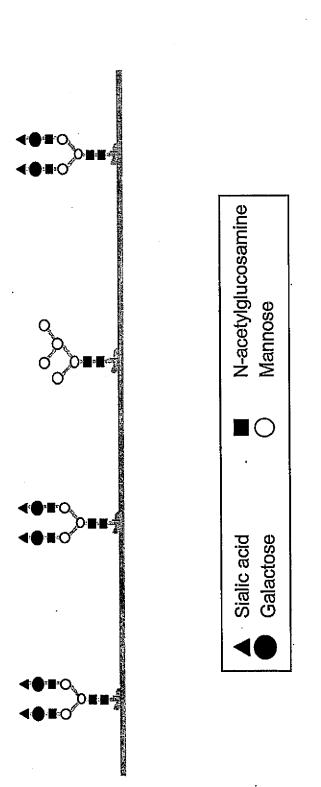
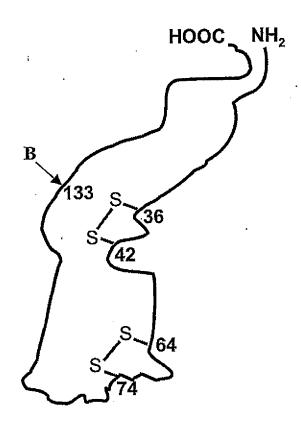


FIG. 26



$$\mathbf{B} \leftarrow \begin{pmatrix} (\mathrm{Sia})_{b} \\ -\mathrm{GalNAc-(Gal)}_{a}-(\mathrm{Sia})_{c}-(\mathrm{R})_{d} \end{pmatrix}_{e}$$

a-c, e (independently selected) = 0 or 1;
d = 0;
R = modifying group, mannose, oligomannose

CHO, BHK, 293 cells, Vero expressed G-CSF a-c, e (independently selected) = 0 or 1; d = 0

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 27B

Insect cell expressed G-CSF a, e (independently selected) = 0 or 1; b, c, d = 0.

- 1. Galactosyltransferase, UDP-Gal
- 2. CMP-SA-PEG, ST3Gal1

a, c, d, e (independently selected) = 0 or 1; R = PEG.

FIG. 27C

E. coli expressed G-CSF a-e=0.

- 1. GalNAc Transferase, UDP-GalNAc
- 2. CMP-SA-PEG, sialyltransferase

c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

FIG. 27D

NSO expressed G-CSF a, e (independently selected) = 0 or 1; b, c, d = 0

- 1. CMP-SA-levulinate, ST3Gal1
- $2. H_4 N_2$ -PEG

a, c, d, e (independently selected) = 0 or 1; b = 0; R = PEG.

FIG. 27E

E. coli expressed G-CSF a-e=0.

1. Endo-GalNAc-osaminidase (synthetic enzyme), PEG-Gal-GalNAc-F

a, d, e = 1; b, c = 0; R = PEG.

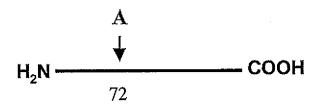
FIG. 27F

E. coli expressed G-CSF a-e = 0.

1. GalNAc Transferase, UDP-GalNAc-PEG

d, e = 0 or 1; a,-c = 0; R = PEG.

FIG. 27G



$$\mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc\text{-}}(\mathrm{Gal})_{a}]_{e}\text{-}(\mathrm{Sia})_{j}\text{-}(\mathrm{R})_{v} \end{bmatrix}_{r} \\ [\mathrm{GlcNAc\text{-}}(\mathrm{Gal})_{b}]_{f}\text{-}(\mathrm{Sia})_{k}\text{-}(\mathrm{R})_{w} \end{bmatrix}_{s} \\ [\mathrm{GlcNAc\text{-}}(\mathrm{Gal})_{b}]_{g}\text{-}(\mathrm{Sia})_{l}\text{-}(\mathrm{R})_{x} \end{bmatrix}_{t} \\ [\mathrm{GlcNAc\text{-}}(\mathrm{Gal})_{d}]_{h}\text{-}(\mathrm{Sia})_{m}\text{-}(\mathrm{R})_{y} \end{bmatrix}_{u}$$

$$\mathbf{B} \leftarrow \begin{pmatrix} (\operatorname{GlcNAc-Gal})_{cc} - (\operatorname{Sia})_{o} - (R)_{ee} \\ - \operatorname{GalNAc-(Gal})_{n} - (\operatorname{Sia})_{p} - (R)_{z} \end{pmatrix}_{q}$$

a-d, i, n-u (independently selected) = 0 or 1.
aa, bb, cc, dd, ee (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 20.
v-z = 0; R = modifying group, mannose, oligo-mannose.
R' = H, glycosyl residue, modifying group,
glycoconjugate.

FIG. 28A

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```
CHO, BHK, 293 cells, Vero expressed interferon alpha 14C.
a-d, aa, bb = 1; e-h = 1 to 4;
cc, j-m, i, r-u (independently selected) = 0 or 1;
q, n-p, v-z, cc, dd, ee = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3

```
a-d, aa, bb = 1; e-h = 1 to 4;
bb, cc, i, r-u (independently selected) = 0 or 1;
q, n-p, v-z, cc, dd, ee = 0;
v-y (independently selected) = 1,
when j-m (independently selected) = 1;
R = PEG.
```

FIG. 28B

```
Insect cell or fungi expressed interferon alpha-14C. a-d, f, h, j-q, s, u, v-z, cc, dd, ee = 0; e, g, i, r, t (independently selected) = 0 or 1; aa, bb = 1.
```

- 1. GNT's 1&2, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

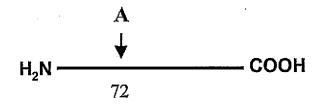
```
b, d, f, h, j-q, s, u, w, y, z, cc, dd, ee = 0;
a, c, e, g, i, r, t, v, x (independently selected) = 0 or 1;
v, x (independently selected) = 1,
when a, c, (independently selected) = 1;
aa, bb = 1; R = PEG.
```

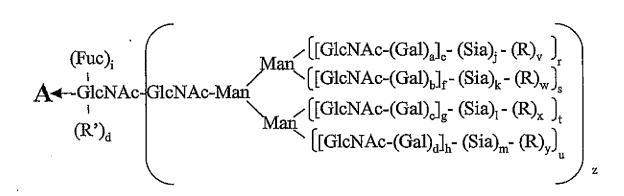
Yeast expressed interferon alpha-14C. a-q, cc, dd, ee, v-z = 0; r-y (independently selected) = 0 to 1; aa, bb = 1;R (branched or linear) = Man, oligomannose or polysaccharide.

- 1. Endo-H
- Galactosyltransferase, UDP-Gal
 CMP-SA-PEG, ST3Gal3

a-z, bb = 0; aa = 1; R' = -Gal-Sia-PEG.

FIG. 28D





a-d, i, r-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y = 0; z = 0 or 1. R = polymer; R' = sugar, glycoconjugate.

FIG. 28E

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```
CHO, BHK, 293 cells, Vero expressed interferon alpha-14C.

h = 1 to 3;

a-g, j-m, i (independently selected) = 0 or 1;

r-u (independently selected) = 0 or 1;

n, v-y = 0; z = 1.
```

1. CMP-SA-PEG, ST3Gal3

```
h = 1 to 3;
a-g, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
j-m, v-y (independently selected) = 0 or 1;
z = 1; n = 0; R = PEG.
```

FIG. 28F

```
Insect cell or fungi expressed
interferon alpha-14C.
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, r, t (independently selected) = 0 or 1;
z = 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

a-m, r-y (independently selected) = 0 or 1; z = 1; n = 0; R = PEG.

FIG. 28G

Yeast expressed interferon alpha-14C. a-n = 0; r-y (independently selected) = 0 to 1; z = 1; R (branched or linear) = Man, oligomannose.

- 1. mannosidases
- 2. GNT's 1,2,4,5, UDP-GlcNAc
- 3. Galactosyltransferase, UDP-Gal
- 4.. CMP-SA-PEG, ST3Gal3

a-m, r-y (independently selected) = 0 or 1; z = 1; n = 0; R = PEG.

FIG. 28H

NSO expressed interferon alpha 14C. a-i, r-u (independently selected) = 0 or 1; j-m, n, v-y = 0; z = 1.

- 1. CMP-SA-levulinate, ST3Gal3, buffer, salt
- $2. H_4N_2$ -PEG

a-i, j-m, r-y (independently selected) = 0 or 1; n = 0; z = 1; R = PEG.

FIG. 281

```
CHO, BHK, 293 cells, Vero expressed interferon alpha-14C.

h = 1 to 3;
a-g, j-m, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
n, v-y = 0; z = 1.
```

1. CMP-SA-PEG, α 2,8-ST

```
h = 1 to 3;
a-g, i, r-u (independently selected) = 0 or 1;
j-m (independently selected) = 0 to 2;
v-y (independently selected) = 1,
when j-m (independently selected) is 2;
z = 1; n = 0; R = PEG.
```

FIG. 28J

```
CHO, BHK, 293 cells, Vero expressed Interferon alpha-14C.
a-g, j-m, r-u (independently selected) = 0 or 1;
h = 1 to 3; n, v-y = 0; z = 1.
```

- 1. Sialidase
- 2. Trans-sialidase, PEG-Sia-lactose

a-g, j-m, r-y (independently selected) = 0 or 1; h = 1 to 3; n = 0; z = 1; R = PEG.

FIG. 28K

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```
CHO, BHK, 293 cells, Vero expressed interferon alpha-14C.

h = 1 to 3;
a-g, j-m, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
n, v-y = 0; z = 1.
```

1. CMP-SA, α 2,8-ST

```
h = 1 to 3;
a-g, i, r-u (independently selected) = 0 or 1;
j-m (independently selected) = 0 to 40;
z = 1; v-y, n = 0.
```

FIG. 28L

```
Insect cell or fungi expressed interferon alpha-14C.
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, r, t (independently selected) = 0 or 1;
z = 1.
```

- 1. GNT's 1 & 2, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-linker-SA-CMP
- 3. ST3Gal3, transferrin

```
a, c, e, g, i, r, t, v, x (independently selected) = 0 or 1;

z = 1; b, d, f, h, j-n, s, u, w, y = 0;

R = \text{transferrin}.
```

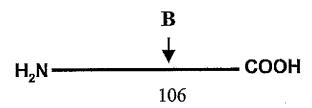
FIG. 28M

```
Insect cell or fungi expressed interferon alpha-14C.
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, r, t (independently selected) = 0 or 1; z = 1.
```

- 1. endoglycanase
- 2. Galactosyltransferase, UDP-Gal-linker-SA-CMP
- 3. ST3Gal3, transferrin

```
i (independently selected) = 0 or 1;
a-h, j-m, r-z = 0;
n = 1; R' = -Gal-linker-transferrin.
```

FIG. 28N



$$\mathbf{B} \leftarrow \begin{pmatrix} (\operatorname{GlcNAc-Gal})_{\mathbf{f}} - (\operatorname{Sia})_{\mathbf{b}} - (\mathbf{R})_{\mathbf{g}} \\ - \operatorname{GalNAc-(Gal)}_{\mathbf{a}} - (\operatorname{Sia})_{\mathbf{c}} - (\mathbf{R})_{\mathbf{d}} \end{pmatrix}_{\mathbf{e}}$$

a-c, e, f (independently selected) = 0 or 1; d, g = 0; R = polymer, glycoconjugate.

FIG. 280

CHO, BHK, 293 cells, Vero expressed IF-alpha (2a or 2b). a-c (independently selected) = 0 or 1; e = 1; d, f, g = 0

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal1

a-d (independently selected) = 0 or 1; e = 1; b, f, g = 0; R = PEG.

FIG. 28P

Insect cell expressed interferon alpha (2a or 2b). a, e (independently selected) = 0 or 1; b, c, d, f, g = 0.

- 1. Galactosyltransferase, UDP-Gal
- 2. CMP-SA-PEG, ST3Gal1

a, c, d, e (independently selected) = 0 or 1; b, f, g = 0; R = PEG.

FIG. 28Q

E. coli expressed IF-alpha (2a or 2b). a-g=0.

1. GalNAc Transferase, UDP-GalNAc-PEG

a-c, f, g = 0; d, e = 1; R = PEG.

FIG. 28R

NSO expressed IF-alpha (2a or 2b). a (independently selected) = 0 or 1; e = 1; b, c, d, f, g = 0

- 1. CMP-SA-levulinate, ST3Gal1
- $2. H_4N_2$ -PEG

a, c, d (independently selected) = 0 or 1; e = 1; b, f, g = 0; R = PEG.

FIG. 28S

E. coli expressed IF-alpha (2a or 2b). a-g=0.

1. Endo-N-acetylgalatosamidase (synthetic enzyme), PEG-Gal-GalNAc-F

a, d, e = 1; b, c, f, g = 0; R = PEG.

FIG. 28T

E. coli expressed IF-alpha (2a or 2b). a-g=0.

- 1. GalNAc Transferase, UDP-GalNAc
- 2. sialyltransferase, CMP-SA-PEG

b, d = 0 or 1; e = 1; a, c, f, g = 0; R = PEG.

FIG. 28U

CHO, BHK, 293 cells, Vero expressed IF-alpha (2a or 2b). a-c, f (independently selected) = 0 or 1; e = 1; d, g = 0

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal1 and ST3Gal3

a-d, f, g (independently selected) = 0 or 1; e = 1; R = PEG.

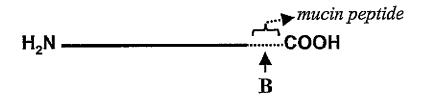
FIG. 28V

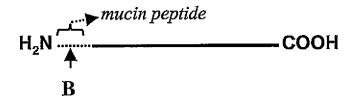
CHO, BHK, 293 cells, Vero expressed IF-alpha (2a or 2b). a-c, f (independently selected) = 0 or 1; e = 1; d, g = 0

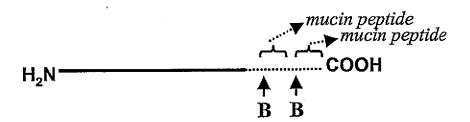
- 1. Sialidase
- 2. CMP-SA-linker-SA-CMP, ,ST3Gal1
- 3. ST3Gal3, transferrin

a-d, f (independently selected) = 0 or 1; e = 1; R = transferrin; g = 0.

FIG. 28W







$$\mathbf{B} \quad \blacktriangleleft \begin{bmatrix} (\mathrm{Sia})_{b} \\ -\mathrm{GalNAc-(Gal)_{a}-(Sia)_{c}-(R)_{d}} \end{bmatrix}_{e}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = polymer, glycoconjugate.

FIG. 28X

CHO, BHK, 293 cells, Vero expressed interferon alpha-mucin fusion protein. a-c, e (independently selected) = 0 or 1; d = 0

- Sialidase
 - 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 28Y

Insect cell expressed interferon alpha-mucin fusion protein.

a, e (independently selected) = 0 or 1; b, c, d = 0.

1. Galactosyltransferase, UDP-Gal-PEG

a, d, e (independently selected) = 0 or 1; b, c = 0; R = PEG.

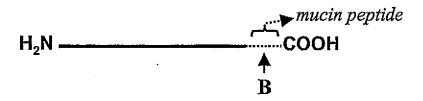
E. coli expressed interferon alpha-mucin fusion protein.

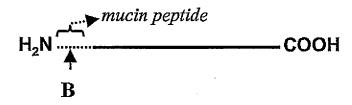
$$a-e=0$$
.

- 1. GalNAc Transferase, UDP-GalNAc
- 2. CMP-SA-PEG, sialyltransferase

c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

FIG. 28AA





$$\mathbf{B} \leftarrow \begin{bmatrix} (\operatorname{Sia})_{b} \\ -\operatorname{GalNAc-(Gal)}_{a} - (\operatorname{Sia})_{c} - (R)_{d} \end{bmatrix}_{e}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = polymer, linker.

FIG. 28BB

E. coli expressed interferon alpha-mucin fusion protein.

a-e, n=0.

1. GalNAc Transferase, UDP-GalNAc-PEG

d, e (independently selected) = 0 or 1; a-c, n = 0; R = PEG.

FIG. 28CC

E. coli expressed interferon alpha-mucin fusion protein.

a-e, n = 0.

- 1. GalNAc Transferase, UDP-GalNAc-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
- 3. CMP-SA, ST3Gal3

d, e (independently selected) = 0 or 1; a-c, n = 0; R = linker-transferrin.

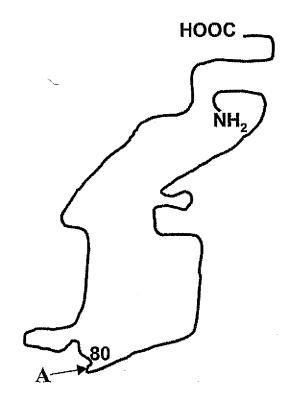
FIG. 28DD

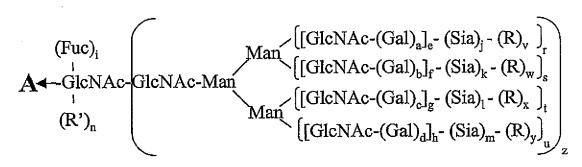
E. coli expressed Interferon alpha (no fusion). a-e, n = 0.

- 1. NHS-CO-linker-SA-CMP
- 2. ST3Gal3, transferrin

a-e=0; n=1; R'=linker-transferrin.

FIG. 28EE





a-d, i, r-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y = 0; z = 0 or 1; R = polymer

FIG. 29A

```
CHO, BHK, 293 cells, Vero expressed IF-beta h = 1 to 3; a-g, j-m, i (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; n, v-y = 0; z = 1.
```

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3

```
h = 1 to 3;
a-g, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
j-m, v-y (independently selected) = 0 or 1;
z = 1; n = 0; R = PEG.
```

FIG. 29B

```
Insect cell expressed IF-beta a-d, f, h, j-n, s, u, v-y = 0; e, g, i, r, t (independently selected) = 0 or 1; z = 1.
```

- 1. GNT's 1&2, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal
- 2. CMP-SA-PEG, ST3Gal3, buffer, salt

```
b, d, f, h, k, m, n, s, u, w, y = 0;
a, c, e, g, i, r, t (independently selected) = 0 or 1;
j, l, v, x (independently selected) = 0 or 1;
z = 1; R = PEG.
```

Yeast expressed IF-beta a-n = 0; z = 1; r-y (independently selected) = 0 to 1; R (branched or linear) = Man, oligomannose or polysaccharide.

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal
- 3.. CMP-SA-PEG, ST3Gal3

a-m, r-z=0; n=1; R'=-Gal-Sia-PEG.

FIG. 29D

```
CHO, BHK, 293 cells, Vero expressed IF-beta h = 1 to 3; a-g, j-m, i (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; n, v-y = 0; z = 1.
```

1. CMP-SA-PEG, ST3Gal3

```
h = 1 to 3;
a-g, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
j-m, v-y (independently selected) = 0 or 1;
z = 1; n = 0; R = PEG.
```

FIG. 29E

Insect cell expressed IF-beta a-d, f, h, j-n, s, u, v-y = 0; e, g, i, r, t (independently selected) = 0 or 1; z = 1.

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal
- 3, CMP-SA-PEG, ST3Gal3

a-m, r-y (independently selected) = 0 or 1; z = 1; n = 0; R = PEG.

FIG. 29F

Yeast expressed IF-beta a-n = 0; z = 1; r-y (independently selected) = 0 to 1; R (branched or linear) = Man, oligomannose.

- 1. mannosidases
- 2. GNT's 1,2,4,5, UDP-GlcNAc
- 3. Galactosyltransferase, UDP-Gal
- 4.. CMP-SA-PEG, ST3Gal3

a-m, r-y (independently selected) = 0 or 1; z = 1; n = 0; R = PEG.

NSO expressed IF-beta a-i, r-u (independently selected) = 0 or 1; j-m, n, v-y = 0; z = 1.

- CMP-SA-levulinate, ST3Gal3, buffer, salt
- 2. H₄N₂-PEG

a-i, j-m, r-y (independently selected) = 0 or 1; n = 0; z = 1; R = PEG.

FIG. 29H

CHO, BHK, 293 cells, Vero expressed IF-beta h = 1 to 3; a-g, j-m, i (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; n, v-y = 0; z = 1.

1. CMP-SA-PEG, α2,8-ST

h = 1 to 3; a-g, i, r-u (independently selected) = 0 or 1; j-m (independently selected) = 0 to 2; v-y (independently selected) = 1, when j-m (independently selected) is 2; z = 1; n = 0; R = PEG.

FIG. 291

CHO, BHK, 293 cells, Vero expressed IF-beta a-g, j-m, r-u (independently selected) = 0 or 1; h = 1 to 3; n, v-y = 0; z = 1.

- 1. Sialidase
- 2. Trans-sialidase, PEG-Sia-lactose

a-g, j-m, r-y (independently selected) = 0 or 1; h = 1 to 3; n = 0; z = 1; R = PEG.

FIG. 29J

CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h=1; n, v-y=0.

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h = 1; n=0; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 29K

```
NSO expressed Ifn-beta.
a-d, i-m, r-u, z (independently selected) = 0 or 1;
e-h = 1; n, v-y = 0;
Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and α-galactosidase
- 2. α -Galactosyltransferase, UDP-Gal
- ▼ 3. CMP-SA-PEG, ST3Gal3

```
a-d, i-m, r-u, z (independently selected) = 0 or 1;
e-h = 1; R = PEG
n = 0; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
```

FIG. 29L

```
CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h=1; n, v-y=0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

```
a-d, i-m, r-u, z (independently selected) = 0 or 1;
e-h = 1; n = 0;
v-y (independently selected) = 0 or 1; R = PEG.
```

FIG. 29M

CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h=1; n, v-y=0.

 CMP-SA-levulinate, ST3Gal3, buffer, salt
 H₄N₂-PEG

a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h = 1; n = 0; v-y (independently selected) = 0 or 1; R = PEG.

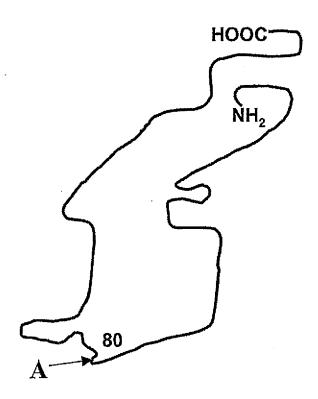
FIG. 29N

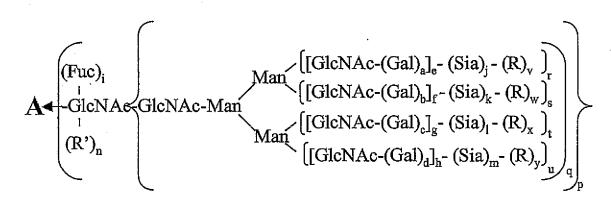
CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h=1; n, v-y=0.

1. CMP-SA, α2,8-ST

a-d, i, r-u, z (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; n, v-y (independently selected) = 0.

FIG. 290





a-d, i, p-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group; R' = H, glycosyl group, modifying group, glycoconjugate.

```
Insect cell expressed Ifn-beta.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1;
j-m = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 29Q

```
Yeast expressed Ifn-beta.

a-m=0; q-y (independently selected) = 0 to 1;

p=1;

R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

```
a-m, p-y = 0;
n (independently selected) = 0 or 1;
R' = -Gal-Sia-PEG.
```

FIG. 29R

CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. CMP-SA-linker-SA-CMP, ST3Gal3
- 2. ST3Gal3, desialylated transferrin.
- 3. CMP-SA, ST3Gal3

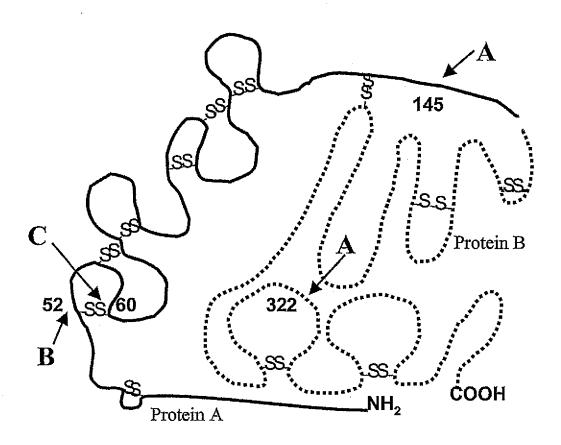
```
a-m, q-u (independently selected) = 0 or 1;

p = 1; n = 0;

v-y (independently selected) = 0 or 1;

R = linker-transferrin.
```

FIG. 29S



$$\mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_a]_e - (\mathrm{Sia})_j - (\mathrm{R})_v \end{bmatrix}_r \\ - \mathrm{GlcNAc} - \mathrm{GlcNAc} - \mathrm{Man} \\ \mathbf{Man} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_b]_f - (\mathrm{Sia})_k - (\mathrm{R})_w \end{bmatrix}_s \\ \mathbf{Man} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_b]_g - (\mathrm{Sia})_l - (\mathrm{R})_x \end{bmatrix}_t \\ \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u \end{bmatrix}_q$$

$$\mathbf{B} \blacktriangleleft \{ \text{Glc-}(\mathbf{X}\mathbf{y}\mathbf{l})_{\mathbf{n}} \}_{\mathbf{0}}$$

$$\mathbf{C}$$
 \leftarrow [-Fuc] $_{\mathbf{p}}$

a-d, i, q-u (independently selected) = 0 or 1. o, p (independently selected) = 0 or 1. e-h, n (independently selected) = 0 to 6. j-m (independently selected) = 0 to 20. v-y = 0; R = modifying group, mannose, oligomannose, Sia-Lewis X, Sia-Lewis A..

FIG. 30A

BHK expressed Factor VII or VIIa a-d, e, i, g, q, j, l, o, p (independently selected) = 0 or 1; r, t = 1; f, h, k, m, s, u, v-y = 0; n = 0-4.

- 1. Sialidase
- 2. CMP-SA-PEG (16 mole eq), ST3Gal3

```
a-d, e, g, i, q, j, l, o, p (independently selected) = 0 or 1;
r, t = 1; f, h, k, m, s, u, w, y = 0; n = 0-4;
v, x, (independently selected) = 1,
when j, l (respectively, independently selected) is 1;
R = PEG.
```

FIG. 30B

CHO, BHK, 293 cells, Vero expressed Factor VII or VIIa a-d, e, i, g, q, j, l, o, p (independently selected) = 0 or 1; r, t = 1; f, h, k, m, s, u, v-y = 0; n = 0-4.

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mole eq), ST3Gal3
- 3. CMP-SA (8 mol eq), ST3Gal3

a-d, e, g, i, q, j, l, o, p (independently selected) = 0 or 1; r, t = 1; f, h, k, m, s, u, w, y = 0; n = 0-4; v or x, (independently selected) = 1, when j or l, (respectively, independently selected) is 1; R = PEG.

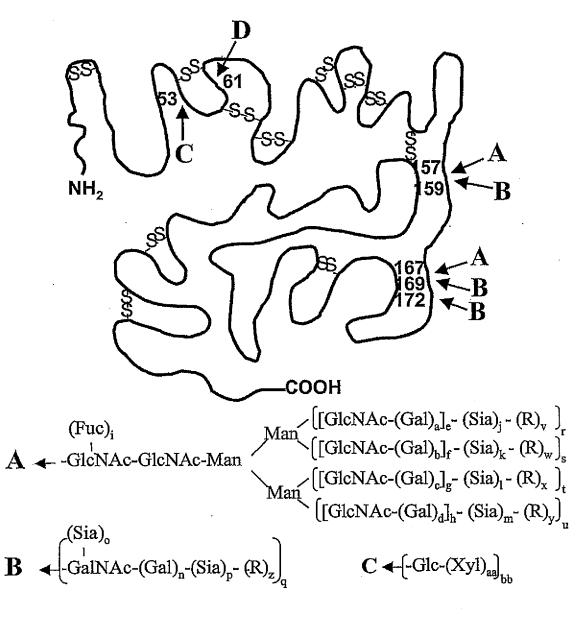
FIG. 30C

```
NSO expressed Factor VII or VIIa
a--u (independently selected) = 0 or 1;
v-y = 0; n = 0-4;
Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and α -galactosidase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

```
a-m, o-u (independently selected) = 0 or 1;
n = 0-4; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
Sia = Sia; R = PEG.
```

FIG. 30D



a-d, i, n-u (independently selected) = 0 or 1.
bb, cc, dd, ee, ff, gg (independently selected) = 0 or 1.
e-h, aa (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 20.
v-z = 0; R = modifying group, mannose, oligo-mannose.

FIG. 31A

```
CHO, BHK, 293 cells, Vero expressed Factor IX a-d, q = 1; e-h = 1 to 4; aa, bb, cc, dd, ee, ff, j-m, i, n, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3

```
a-d, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected)
= 0 or 1;
o, p, z = 0;
j-m, ee, v-y, gg (independently selected) = 0 or 1;
R = PEG.
```

FIG. 31B

```
CHO, BHK, 293 cells, Vero expressed Factor IX a-d, n, q = 1; e-h = 1 to 4; aa, bb, cc, dd, ee, ff, j-m, i, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3
- 3. ST3Gal1, CMP-SA

```
a-d, n, p, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, i, r-u (independently selected) = 0 or 1;
j-m, ee, v-y, gg (independently selected) = 0 or 1;
o, z = 0; R = PEG.
```

FIG. 31C

CHO, BHK, 293 cells, Vero expressed Factor IX a-d, n, q, bb, cc, dd, ff = 1; e-h, aa = 1 to 4; ee, j-m, i, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.

- 1. sialidase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA, ST3Gal3
- 4. CMP-SA-PEG, ST3Gal1

```
a-d, n, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, i, r-u (independently selected) =
0 or 1; R = PEG;
o, v-y, gg = 0;
j-m, p, ee (independently selected) = 0 or 1, but when
p = 1, z = 1.
```

FIG. 31D

```
CHO, BHK, 293 cells, Vero expressed Factor IX a-d, q = 1; e-h = 1 to 4; aa, bb, cc, dd, ee, ff, j-m, i, n, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.
```

CMP-SA-PEG, ST3Gal3

a-d, q = 1; e-h = 1 to 4; aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected) = 0 or 1; R = PEG; o, p, z = 0; j-m, ee, v-y, gg (independently selected) = 0 or 1.

FIG. 31E

```
CHO, BHK, 293 cells, Vero expressed Factor IX a-d, q = 1; e-h = 1 to 4; aa, bb, cc, dd, ee, ff, j-m, i, n, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.
```

 CMP-SA-levulinate, ST3Gal3, buffer, salt
 H₄N₂-PEG

```
a-d, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected)
= 0 or 1;
o, p, z = 0; R = PEG;
j-m, ee, v-y, gg (independently selected) = 0 or 1.
```

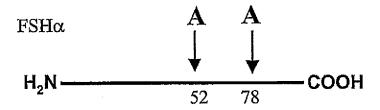
FIG. 31F

```
CHO, BHK, 293 cells, Vero expressed Factor IX
a-d, n, q, bb, cc, dd, ff = 1;
e-h, aa = 1 to 4;
ee, j-m, i, o, p, r-u (independently selected) = 0 or 1;
v-z, gg = 0.
```

1. CMP-SA-PEG, α 2,8-ST

```
a-d, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected) = 0 or 1;
o, p, z = 0; R= PEG;
j-m, ee (independently selected) = 0 to 2;
v-y, gg (independently selected) = 1, when j-m (independently selected) is 2;
```

FIG. 31G



$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{a})_{e} - (\operatorname{Sia})_{j} - (\operatorname{R})_{v} \\ (\operatorname{GlcNAc-GlcNAc-Man})_{f} - (\operatorname{Sia})_{k} - (\operatorname{R})_{w} \end{bmatrix}_{s} \\ = \underbrace{\begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{b})_{f} - (\operatorname{Sia})_{k} - (\operatorname{R})_{w} \\ (\operatorname{GlcNAc-(Gal)}_{c})_{g} - (\operatorname{Sia})_{l} - (\operatorname{R})_{x} \\ (\operatorname{[GlcNAc-(Gal)}_{d}]_{h} - (\operatorname{Sia})_{m} - (\operatorname{R})_{y} \end{bmatrix}_{u}}_{q}$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group, mannose, oligo-mannose.

FIG. 32A

CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.

FIG. 32B

CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG. WO 03/031464 PCT/US02/32263

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NSO expressed FSH.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0;

Sia (independently selected) = Sia or Gal.

- 1. Sialidase and α-galactosidase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal1

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.

FIG. 32D

CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 32E

CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. CMP-SA-levulinate, ST3Gal3, buffer, salt
- 2. H₄N₂-PEG

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 32F

CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 32G

```
Insect cell expressed FSH.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1;
j-m = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 32H

```
Yeast expressed FSH.

a-m = 0; q-y (independently selected) = 0 to 1;

p = 1;

R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

```
a-m, p-y = 0;
n (independently selected) = 0 or 1;
R' = -Gal-Sia-PEG.
```

```
CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- 1. CMP-SA-linker-SA-CMP, ST3Gal3
- 2. ST3Gal1, desialylated chorionic gonadrophin (CG) produced in CHO.
- 3. CMP-SA, ST3Gal3, ST3Gal1

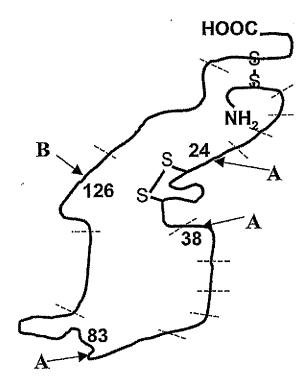
```
a-m, q-u (independently selected) = 0 or 1;

p = 1; n = 0;

v-y (independently selected) = 0 or 1;

R = linker-CG.
```

FIG. 32J



$$\mathbf{A} \leftarrow \text{-GlcNAc-GlcNAc-Man} \qquad \begin{bmatrix} [\text{GlcNAc-(Gal)}_a]_e - (\text{Sia})_j - (R)_v \end{bmatrix}_r \\ -\text{GlcNAc-GlcNAc-Man} \\ \boxed{\begin{bmatrix} [\text{GlcNAc-(Gal)}_b]_f - (\text{Sia})_k - (R)_w \end{bmatrix}_s} \\ \boxed{\begin{bmatrix} [\text{GlcNAc-(Gal)}_c]_g - (\text{Sia})_l - (R)_x \end{bmatrix}_t} \\ \boxed{\begin{bmatrix} [\text{GlcNAc-(Gal)}_d]_h - (\text{Sia})_m - (R)_y \end{bmatrix}_u} \\ \boxed{\begin{bmatrix} [\text{GlcNAc-(Gal)}_d]_h - (\text{Sia})_m - (R)_y \end{bmatrix}_u} \\ \boxed{\begin{bmatrix} (\text{Sia})_o \\ -\text{GalNAc-(Gal)}_n - (\text{Sia})_p - (R)_z \end{bmatrix}_a} \\ \boxed{\mathbf{B}} \leftarrow \begin{bmatrix} (\text{Sia})_o \\ -\text{GalNAc-(Gal)}_n - (\text{Sia})_p - (R)_z \end{bmatrix}_a}$$

a-d, i, n-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 to 20. v-z = 0;

R = modifying group, mannose, oligo-mannose.

FIG. 33A

```
CHO, BHK, 293 cells, Vero expressed EPO a-g, n, q = 1; h = 1 to 3; j-m, i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 to 1; v-z = 0
```

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3

```
a-g, n, q = 1; h = 1 to 3;
i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
j-m, v-y (independently selected) = 0 or 1;
R = PEG; z = 0.
```

FIG. 33B

```
Insect cell expressed EPO a-d, f, h, j-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1&2, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal
- 2. CMP-SA-PEG, ST3Gal3

b, d, f, h, k, m-q, s, u, w, y, z = 0; a, c, e, g, i, r, t (independently selected)= 0 or 1; j, 1, v, x (independently selected) = 0 or 1; R = PEG.

```
CHO, BHK, 293 cells, Vero expressed EPO a-q, r-u (independently selected) = 0 or 1; v-z = 0.
```

- 1. sialidase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA, ST3Gal3
- 4. CMP-SA-PEG, ST3Gal1

```
a-h, n, q = 1;
i-m, o, r-u (independently selected) = 0 or 1;
v-y = 0; p, z = 0 or 1; R = PEG.
```

FIG. 33D

```
CHO, BHK, 293 cells, Vero expressed EPO a-g, n, q = 1; h = 1 to 3; j-m, i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; v-z = 0
```

1. CMP-SA-PEG, ST3Gal3

```
a-g, n, q = 1; h = 1 to 3;
i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 to 1;
j-m, v-y (independently selected) = 0 or 1;
R = PEG; z = 0.
```

FIG. 33E

Insect cell expressed EPO a-d, f, h, j-m, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.

- 1. GNT's 1, 2 & 5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

a-c, e-g, n, q-t, v-x, z (independently selected) = 0 or 1; d, h, j-m, o, p, y, z = 0; R = PEG.

FIG. 33F

Insect cell expressed EPO a-d, f, h, j-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.

- 1. GNT's 1, 2 & 5, UDP-GlcNAc
- 2. Galactosidase (synthetic enzyme), PEG-Gal-F.

a-c, e-g, n, q-t, v-x, z (independently selected) = 0 or 1; d, h, j-m, o, p, y, z = 0; R = PEG.

FIG. 33G

```
NSO expressed NESP
q = 1; a-i, n, r-u (independently selected) = 0
or 1; j-m, o, p, v-z = 0

1. CMP-SA-levulinate, ST3Gal3,
buffer, salt
2. H<sub>4</sub>N<sub>2</sub>-PEG

q = 1; a-i, j-n, r-y (independently selected) =
0 or 1;
o, p, z = 0; R = PEG.
```

FIG. 33H

```
CHO, BHK, 293 cells, Vero expressed NESP a-g, n, q = 1; h = 1 to 3; j-m, i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; v-z = 0
```

1. CMP-SA-PEG, α 2,8-ST

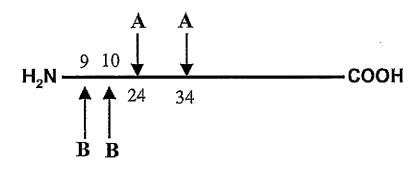
```
a-g, n, q = 1; h = 1 to 3;
i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 to 1;
j-m (independently selected) = 0 to 2;
v-y (independently selected) = 1,
when j-m (independently selected) is 2;
R = PEG; z = 0.
```

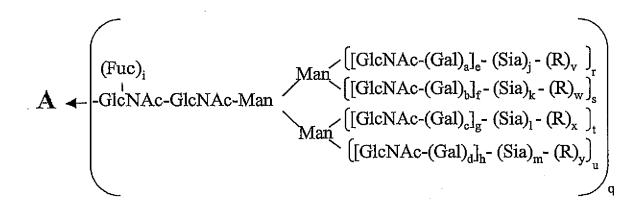
CHO, BHK, 293 cells, Vero expressed NESP a-g, n, q = 1; h = 1 to 3; j-m, i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 to 1; v-z=0

1. CMP-SA, poly- α 2,8-ST

a-g, n, q = 1; h = 1 to 3; i, j-m, o, p, r-u, (independently selected) = 0 or 1; v-z (independently selected) = 0-40; R = Sia.

FIG. 33J





$$\mathbf{B} \leftarrow \begin{bmatrix} (\mathrm{Sia})_{o} \\ -\mathrm{GalNAc-(Gal)}_{n} - (\mathrm{Sia})_{p} - -(\mathrm{R})_{z} \end{bmatrix}_{aa}$$

a-d, i, n-u, aa (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer, glycoconjugate.

FIG. 34A

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CHO, BHK, 293 cells, Vero expressed GM-CSF. a-d, i-m, o-u, as (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

```
a-d, i-m, q-u, aa (independently selected) = 0 or 1;
o, p, z = 0; n, e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 34B

CHO, BHK, 293 cells, Vero expressed GM-CSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- ★ 3. CMP-SA (16 mol eq), ST3Gal3 &
 ST3Gal1

a-d, i-m, p-u, aa (independently selected) = 0 or 1; o, z = 0; n, e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 34C

NSO expressed GM-CSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0; Sia (independently selected) = Sia or Gal.

- 1. Sialidase and α-galactosidase
- 2. CMP-SA, ST3Gal3
- 2. CMP-SA-PEG, ST3Gal1

a-d, i-m, p-u, z, aa (independently selected) = 0 or 1; n, e-h = 1; o, v-y = 0; z = 1, when p = 1; R = PEG.

FIG. 34D

CHO, BHK, 293 cells, Vero expressed GM-CSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

a-d, i-m, q-y, as (independently selected) = 0 or 1; o, p, z = 0; n, e-h = 1; R = PEG.

FIG. 34E

CHO, BHK, 293 cells, Vero expressed GM-CSF. a-d, i-m, o-u, as (independently selected) = 0 or 1; n, e-h = 1; v-z=0.

- 1. CMP-SA-levulinate, ST3Gal3, buffer, salt
- 2. H₄N₂-PEG

a-d, i-m, o-y, aa (independently selected) = 0 or 1; z = 0; n, e-h = 1; R = PEG.

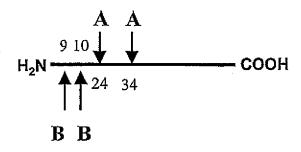
FIG. 34F

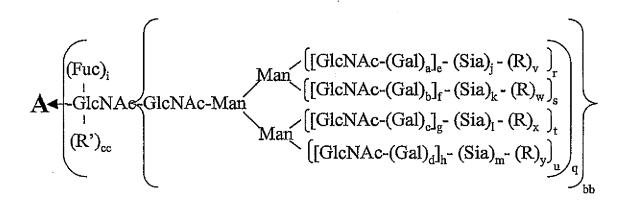
CHO, BHK, 293 cells, Vero expressed GMCSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z=0.

1. CMP-SA, α2,8-ST

a-d, i, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; j-m (independently selected) = 0-20; v-z (independently selected) = 0.

FIG. 34G





$$\mathbf{B}$$

$$\bullet \left(\begin{array}{c} (\mathrm{Sia})_{o} \\ -\mathrm{GalNAc-(Gal)}_{n} - (\mathrm{Sia})_{p} - (\mathrm{R})_{z} \end{array} \right)_{aa}$$

a-d, i, n-u, aa, bb, cc (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group, mannose, oligo-mannose. R'= H, glycosyl residue, modifying group. glycoconjugate.

FIG. 34H

```
Insect cell expressed GM-CSF.
a-d, f, h, j-m, o, p, s, u, v-z = 0;
e, g, i, n, q, r, t, aa (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, n, q-u (independently selected) = 0 or 1;
j-m = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 341

```
Yeast expressed GM-CSF.

a-p, z, cc = 0;

q-y, aa (independently selected) = 0 to 1;

bb = 1; R (branched or linear) = Man, oligomannose;

GalNAc = Man.
```

- 1. Endoglycanase
- 2. mannosidase (if aa = 1).
- 3. Galactosyltransferase, UDP-Gal-PEG

```
a-p, r-z, aa, bb = 0;
q, cc (independently selected) = 0 or 1;
R' = -Gal-PEG.
```

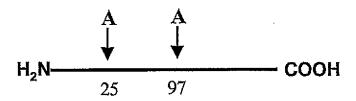
FIG. 34J

CHO, BHK, 293 cells, Vero expressed GM-CSF. a--m, o-u, aa, bb (independently selected) = 0 or 1; n, v-z, cc = 0.

- 1. sialidase
- 2. CMP-SA, ST3Gal3
- 2. CMP-SA-linker-SA-CMP, ST3Gal1
- 3. ST3Gal3, transferrin

a--m, p-u, z, as (independently selected) = 0 or 1; o, v-y, cc = 0; bb, n = 1; R = transferrin.

FIG. 34K



$$\mathbf{A} \leftarrow \begin{bmatrix} \left[\operatorname{GlcNAc-(Gal)}_{a} \right]_{e^{-}} \left(\operatorname{Sia}_{j^{-}} \left(\operatorname{R} \right)_{v^{-}} \right)_{r} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{b} \right]_{f^{-}} \left(\operatorname{Sia}_{k^{-}} \left(\operatorname{R} \right)_{w^{-}} \right)_{s} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{c} \right]_{g^{-}} \left(\operatorname{Sia}_{l^{-}} \left(\operatorname{R} \right)_{x^{-}} \right)_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia}_{m^{-}} \left(\operatorname{R} \right)_{y^{-}} \right)_{u^{-}} \right]_{q} \end{bmatrix}$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

FIG. 35A

```
CHO, BHK, 293 cells, Vero expressed IF-gamma. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 35B

```
CHO, BHK, 293 cells, Vero expressed IF-gamma. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

```
NSO expressed Interferon gamma.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0;

Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and α-galactosidase
- 2. α-Galactosyltransferase, UDP-Gal
- **★** 3. CMP-SA-PEG, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 35D

```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

- 1. Sialidase
- CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 35E

```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

- 1. CMP-SA-levulinate, ST3Gal3,
- 2. H₄N₂-PEG

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

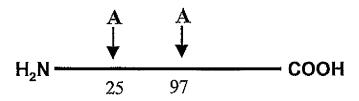
FIG. 35F

```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 35G



$$\mathbf{A} \leftarrow \begin{bmatrix} [\operatorname{GlcNAc-(Gal)}_a]_e - (\operatorname{Sia})_j - (\operatorname{R})_v \\ [\operatorname{GlcNAc-(Gal)}_b]_f - (\operatorname{Sia})_k - (\operatorname{R})_w \end{bmatrix}_r \\ \begin{bmatrix} [\operatorname{GlcNAc-(Gal)}_b]_f - (\operatorname{Sia})_k - (\operatorname{R})_w \end{bmatrix}_s \\ [\operatorname{GlcNAc-(Gal)}_b]_g - (\operatorname{Sia})_l - (\operatorname{R})_x \end{bmatrix}_t \\ \begin{bmatrix} [\operatorname{GlcNAc-(Gal)}_d]_h - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \end{bmatrix}_q$$

a-d, i, n, p-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 35H

```
Insect or fungi cell expressed IF-gamma.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1;
j-m = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 351

```
Yeast expressed IF-gamma.

a-m = 0; q-y (independently selected) = 0 to 1; p = 1;

R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

```
a-m, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.
```

FIG. 35J

```
CHO, BHK, 293 cells, Vero expressed IF-gamma. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- 1. CMP-SA-linker-Gal-UDP, ST3Gal3
- 2. Galactosyltransferase, transferrin treated with endoglycanase.

```
a-m, q-u (independently selected) = 0 or 1;

p = 1; n = 0;

v-y (independently selected) = 0 or 1;

R = linker-transferrin.
```

FIG. 35K

```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h, p = 1; n, v-y = 0.
```

1. CMP-SA-PEG, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h, p = 1;
n, v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 35L

```
Insect or fungi cell expressed IF-gamma.

a-d, f, h, j-n, s, u, v-y = 0;

e, g, i, q, r, t (independently selected) = 0 or 1.
```

1. GNT's 1 & 2, UDP-GlcNAc-PEG

```
a-d, f, h, j-n, s, u, w, y = 0;
e, g, i, r, t, q (independently selected) = 0 or 1;
p = 1; v, x (independently selected) = 1,
when e, g (independently selected) is 1;
R = PEG.
```

FIG. 35M

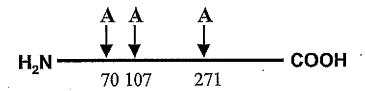
```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

1. CMP-SA-PEG, α 2,8-ST

```
a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1; j-m (independently selected) = 0-2;
v-y (independently selected) = 1,
when j-m (independently selected) = 2;
R = PEG.
```

FIG. 35N

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$$\mathbf{A} \leftarrow \begin{bmatrix} \left[\operatorname{GlcNAc-(Gal)}_{a} \right]_{e^{-}} \left(\operatorname{Sia} \right)_{j} - \left(\operatorname{R} \right)_{v} \right]_{r} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{b} \right]_{f^{-}} \left(\operatorname{Sia} \right)_{k} - \left(\operatorname{R} \right)_{w} \right]_{s} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{b} \right]_{g^{-}} \left(\operatorname{Sia} \right)_{l^{-}} \left(\operatorname{R} \right)_{x} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \end{bmatrix}_{q}$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

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```
CHO, BHK, 293 cells, Vero or transgenic animal expressed \alpha_1 antitrypsin. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 36B

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed \alpha_1 antitrypsin. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 36C

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```
NSO expressed \alpha_1-antitrypsin.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0;

Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and α-galactosidase
- 2. α-Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 36D

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed alpha-1 antitrypsin.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 36E

CHO, BHK, 293 cells, Vero or transgenic animal expressed α₁-antitrypsin.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

- 1. CMP-SA-levulinate, ST3Gal3, buffer, salt
- $2. H_4 N_2$ -PEG

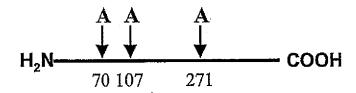
a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 36F

CHO, BHK, 293 cells, Vero expressed α_1 -antitrypsin. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.



$$\mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc-(Gal)_a]_c - (Sia)_j - (R)_v} \\ [\mathrm{GlcNAc-(Gal)_b]_f - (Sia)_k - (R)_w} \end{bmatrix}_r \\ [\mathrm{GlcNAc-(Gal)_b]_f - (Sia)_k - (R)_w} \end{bmatrix}_s \\ [\mathrm{GlcNAc-(Gal)_b]_f - (Sia)_h - (R)_w} \end{bmatrix}_t \\ [\mathrm{GlcNAc-(Gal)_d]_h - (Sia)_m - (R)_y} \end{bmatrix}_u q_p$$

a-d, i, n, p-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0;
R = modifying group, mannose, oligo-mannose;
R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 36H

```
Insect or fungi cell expressed \alpha_1-antitrypsin.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1; j-m = 0;
v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 361

```
Yeast expressed \alpha_1-antitrypsin.

a-m=0; q-y (independently selected) = 0 to 1;

p=1; R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

a-m, p-y=0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.

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CHO, BHK, 293 cells, Vero expressed α_1 -antitrypsin. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

- 1. CMP-SA-linker-Gal-UDP, ST3Gal3
- 2. Galactosyltransferase, transferrin treated with endoglycanase

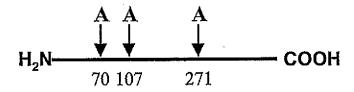
```
a-m, q-u (independently selected) = 0 or 1;

p = 1; n = 0;

v-y (independently selected) = 0 or 1;

R = linker-transferrin.
```

FIG. 36K



$$(Fuc)_{i}$$

$$-GlcNAc-GlcNAc-Man$$

$$(R')_{p}$$

$$(R')_{q}$$

$$(Fuc)_{i}$$

$$-(GlcNAc-(Gal)_{a}]_{e}-(Sia)_{i}-(R)_{v}$$

$$-(GlcNAc-(Gal)_{b}]_{f}-(Sia)_{k}-(R)_{w}$$

$$-(GlcNAc-(Gal)_{c}]_{g}-(Sia)_{l}-(R)_{x}$$

$$-(GlcNAc-(Gal)_{c}]_{g}-(Sia)_{l}-(R)_{x}$$

$$-(GlcNAc-(Gal)_{c}]_{g}-(Sia)_{l}-(R)_{v}$$

$$-(GlcNAc-(Gal)_{d}]_{h}-(Sia)_{m}-(R)_{v}$$

$$-(GlcNAc-(Gal)_{d}]_{h}-(Sia)_{m}-(R)_{v}$$

a-d, i, n-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4.

j-m (independently selected) = 0 to 20.

R = polymer;

R', R" (independently selected) = sugar, glycoconjugate.

Yeast expressed alpha-1 antitrypsin. a-h, i-m, p, q = 0; R (independently selected) = mannose, oligomannose, polymannose; r-u, v-y (independently selected) = 0 or 1; n, o = 1.

- 1. endoglycanase
- 2. Galactosyltransferase, UDP-Gal-PEG

a-h, i-o, q, r-u, v-y = 0; p = 1. R" = Gal-PEG.

FIG. 36M

Plant expressed alpha-1 antitrypsin. a-d, f, h, j-m, s, u, v-y = 0; e, g, i, q, r, t (independently selected) = 0 or 1; n=1; R' = xylose

- 1. hexosaminidase,
- 2. alpha mannosidase and xylosidase
- 3. GlcNAc transferase, UDP-GlcNAc-PEG

a-d, f, h, j-n, s, u, v-y = 0; e, g, i, r, t (independently selected) = 0; q = 1; R' = GlcNAc-PEG. PCT/US02/32263

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CHO, BHK, 293 cells, Vero, transgenic animal expressed α₁ antitrypsin.
a-h, i-o, r-u (independently selected) = 0 or 1;
p, q, v-y = 0.

1. CMP-SA-PEG, ST3Gal3

a-h, i-o, r-u (independently selected) = 0 or 1; p, q = 0; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 360

$$\mathbf{A} \leftarrow \begin{bmatrix} \left[\operatorname{GlcNAc-(Gal)}_{a} \right]_{e^{-}} \left(\operatorname{Sia} \right)_{j} - \left(\operatorname{R} \right)_{v} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{b} \right]_{f^{-}} \left(\operatorname{Sia} \right)_{k^{-}} - \left(\operatorname{R} \right)_{w} \right]_{s} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{b} \right]_{g^{-}} \left(\operatorname{Sia} \right)_{l^{-}} \left(\operatorname{R} \right)_{x} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{n} \end{bmatrix}_{q}$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

FIG. 37A

CHO, BHK, 293 cells, Vero expressed Cerezyme a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 37B

```
CHO, BHK, 293 cells, Vero expressed Cerezyme. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- 1. Sialidase
- 2. CMP-SA-M-6-P (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = mannose-6-phosphate

```
NSO expressed Cerezyme.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0;

Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and α-galactosidase
- 2. α-Galactosyltransferase, UDP-Gal
- **▼** 3. CMP-SA-M-6-P, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = mannose-6 phosphate
```

FIG. 37D

```
CHO, BHK, 293 cells, Vero expressed Cerezyme. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = Mannose-6-phosphate
```

FIG. 37E

CHO, BHK, 293 cells, Vero expressed Cerezyme. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. CMP-SA-levulinate, ST3Gal3, buffer, salt
- 2. H₄N₂-spacer-M-6-P or clustered M-6-P

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = M-6-P or clustered M-6-P

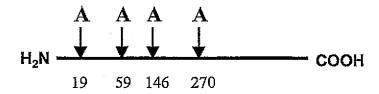
FIG. 37F

CHO, BHK, 293 cells, Vero expressed Cerezyme. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 37G



$$\mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc\text{-}}(\mathrm{Gal})_a]_e - (\mathrm{Sia})_j - (\mathrm{R})_v \end{bmatrix}_r \\ [\mathrm{GlcNAc\text{-}}(\mathrm{Gal})_b]_f - (\mathrm{Sia})_k - (\mathrm{R})_w \end{bmatrix}_s \\ [\mathrm{GlcNAc\text{-}}(\mathrm{Gal})_b]_g - (\mathrm{Sia})_l - (\mathrm{R})_x \end{bmatrix}_t \\ [\mathrm{GlcNAc\text{-}}(\mathrm{Gal})_d]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u = 0$$

a-d, i, n, p-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 37H

```
Insect cell expressed Cerezyme.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1;

j-m = 0;

v-y (independently selected) = 1,

when e-h (independently selected) is 1;

R = PEG.
```

FIG. 371

```
Yeast expressed Cerezyme.

a-m = 0; q-y (independently selected) = 0 to 1;

p = 1; R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

a-m, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.

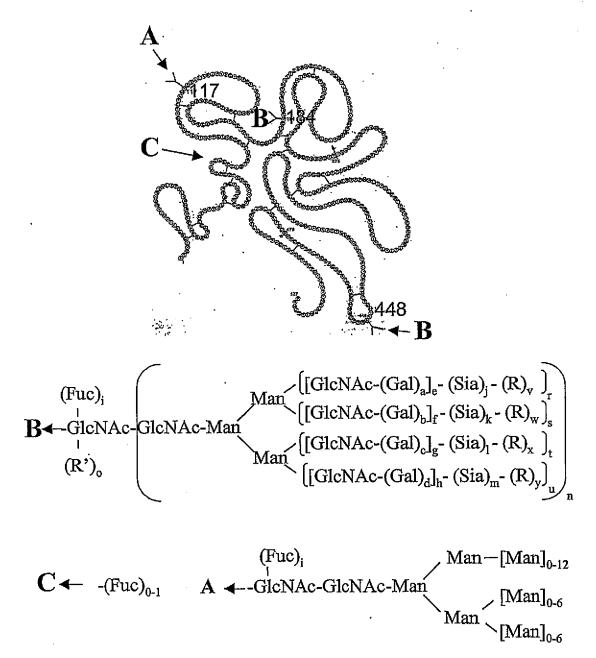
FIG. 37J

CHO, BHK, 293 cells, Vero expressed Cerezyme. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. CMP-SA-linker-SA-CMP, ST3Gal3
- 2. ST3Gal3, desialylated transferrin.
- 3. CMP-SA, ST3Gal3

a-m, q-u (independently selected) = 0 or 1; p = 1; n = 0; v-y (independently selected) = 0 or 1; R = linker-transferrin.

FIG. 37K



a-d, i, n-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 to 20. R = polymer; R' = sugar, glycoconjugate.

FIG. 38A

WO 03/031464 PCT/US02/32263

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```
CHO, BHK, 293 cells, Vero expressed tPA a-g, n = 1; h = 1 to 3; j-m, i, (independently selected) = 0 or 1; r-u (independently selected) = 0 to 1; o, v-y = 0.
```

- 1. Mannosidase(s), sialidase
- 2. GNT1,2 (4 and/or 5) UDP-GlcNAc
- 3. Gal transferase, UDP-Gal
- 4. CMP-SA-PEG, ST3Gal3

```
A = B; a-g, n = 1; h = 1 to 3;
i, r-u (independently selected) = 0 or 1;
o = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG
```

FIG. 38B

```
Insect or fungi cell expressed tPA
A = B; a-d, f, h, j-o, s, u, v-y = 0;
e, g, i, n, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1&2, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal
- ♦ 3. CMP-SA-PEG, ST3Gal3

```
A=B; b, d, f, h, k, m, o, s, u, w, y = 0;
a, c, e, g, i, r, t (independently selected) = 0 or 1;
n = 1; j, l, v, x (independently selected) = 0 or 1;
R = PEG.
```

FIG. 38C

Yeast expressed tPA B = A; i = 0.

- 1. endoglycanase
- 2. Galactosyltransferase, UDP-Gal-PEG

$$A = B$$
; a-n, r-y = 0; $o = 1$; $R' = Gal-PEG$.

FIG. 38D

Insect or fungi cell expressed tPA A = B; a-d, f, h, j-o, s, u, v-y = 0; e, g, i, n, r, t (independently selected) = 0 or 1.

- 1. alpha and beta mannosidases
- 2. Galactosyltransferase, UDP-Gal-PEG

$$A = B$$
; a-n, r-y = 0; o = 1; R' = Gal-PEG.

Insect or fungi cell expressed tPA A = B; a-d, f, h, j-o, s, u, v-y = 0; e, g, i, n, r, t (independently selected) = 0 or 1.

- 1. GNT's 1&2, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

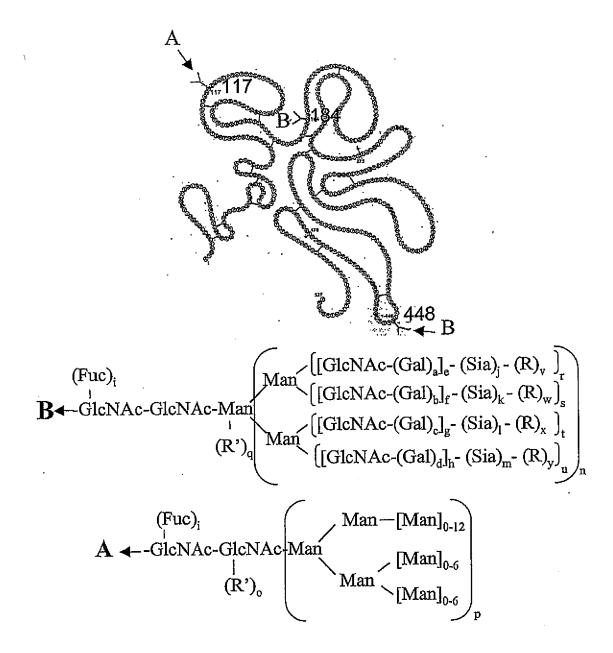
A = B; b, d, f, h, j-o, s, u, w, y = 0; a, c, e, g, i, r, t, v, x (independently selected)= 0 or 1; n = 1; R = PEG.

FIG. 38F

Insect or fungi cell expressed tPA A = B; a-d, f, h, j-o, s, u, v-y = 0; e, g, i, n, r, t (independently selected) = 0 or 1.

- 1. GNT's 1 & 2, UDP-GlcNAc
- 2. Galactosidase (synthetic enzyme), PEG-Gal-F.

A = B; b, d, f, h, j-o, s, u, w, y = 0; a, c, e, g, i, r, t, v, x (independently selected)= 0 or 1; n = 1; R = PEG.



a-d, i, n-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 to 20. R = polymer; R' = sugar, glycoconjugate.

FIG. 38H

```
NSO expressed tPA

A = B; a-m, r-u (independently selected) = 0 or 1;

n = 1; o, p, q, v-y = 0
```

- 1. sialidase, alpha-galactosidase
- 2. CMP-SA-levulinate, ST3Gal3,
- $3. H_4N_2$ -PEG

```
A = B; a-m, r-y (independently selected) = 0 or 1;

n = 1; o, p, q = 0;

v-y (independently selected) = 1,

when j-m (independently selected) is 1;

R = PEG.
```

FIG. 381

```
CHO, BHK, 293 cells, Vero expressed tPA a-g, n, p = 1; h = 1 to 3; j-m, i, (independently selected) = 0 or 1; r-u (independently selected) = 0 to 1; q, o, v-y = 0.
```

- 1. alpha and beta Mannosidases
- 2. CMP-SA, ST3Gal3
- 3. Galactosyltransferase, UDP-Gal-PEG

```
a-g, n = 1; h = 1 to 3;
i, r-u (independently selected) = 0 or 1; o = 1;
q, p, v-y = 0; j-m (independently selected) = 0 or 1;
R' = Gal-PEG
```

FIG. 38J

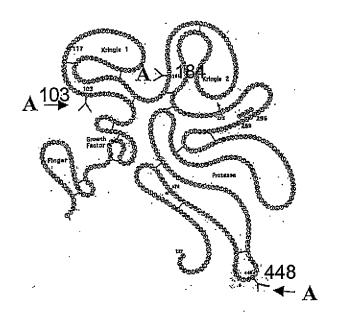
```
Plant expressed tPA

A = B; a-d, f, h, j- m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1;
n = 1; R' = xylose
```

- 1. hexosaminidase,
- 2. alpha mannosidase and xylosidase
- 3. GlcNAc transferase, UDP-GlcNAc-PEG

```
A = B; a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, r, t (independently selected) = 0;
q = 1; R' = GlcNAc-PEG.
```

FIG. 38K



$$\mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc\text{-}(Gal)}_a]_e - (\mathrm{Sia})_j - (\mathrm{R})_v \end{bmatrix}_r \\ - \mathrm{GlcNAc\text{-}GlcNAc\text{-}Man} \\ - \mathrm{GlcNAc\text{-}GlcNAc\text{-}Man} \\ - \mathrm{GlcNAc\text{-}(Gal)}_b]_f - (\mathrm{Sia})_k - (\mathrm{R})_w \end{bmatrix}_s \\ - \mathrm{GlcNAc\text{-}(Gal)}_b \\ - \mathrm{GlcNAc\text{$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

FIG. 38L

CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 1, when j-m (independently selected) is 1; R = PEG.

FIG. 38M

CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. Sialidase
- CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

```
NSO expressed TNK tPA

a-d, i-m, q-u (independently selected) = 0 or 1;

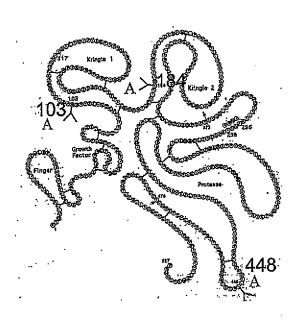
e-h = 1; v-y = 0;

Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and α -galactosidase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 380



$$\mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_a]_e - (\mathrm{Sia})_j - (\mathrm{R})_v \end{bmatrix}_r \\ [\mathrm{GlcNAc} - (\mathrm{Gal})_b]_f - (\mathrm{Sia})_k - (\mathrm{R})_w \end{bmatrix}_s \\ [\mathrm{GlcNAc} - (\mathrm{Gal})_b]_g - (\mathrm{Sia})_l - (\mathrm{R})_x \end{bmatrix}_t \\ [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 38Q

CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

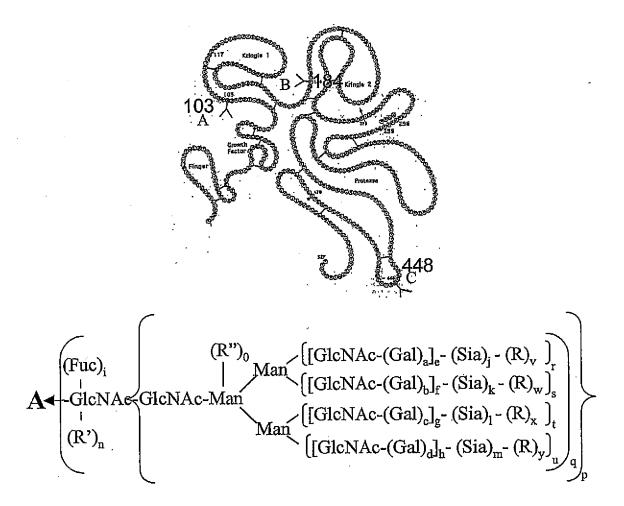
- CMP-SA-levulinate, ST3Gal3, buffer, salt
 H₄N₂-PEG
- a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 38S



a-d, i, n-y (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
R = modifying group, mannose, oligo-mannose;
R' = H, glycosyl residue, modifying group, glycoconjugate.
R" = glycosyl residue.

FIG. 38T

```
Insect cell expressed TNK tPA
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1;
j-m = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 38U

```
Yeast expressed TNK tPA
a-m = 0; q-y (independently selected) = 0 to 1; p = 1;
R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-m, p-y=0; n (independently selected) = 0 or 1; R' = -Gal-PEG.
```

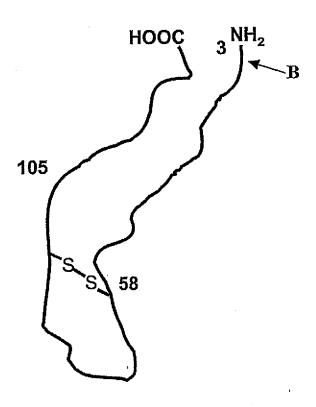
FIG. 38V

CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. CMP-SA-linker-Gal-UDP, ST3Gal3
- 2. Galactosyltransferase, anti-TNF IG chimera produced in CHO.

a-m, r-u (independently selected) = 0 or 1; p, q = 1; n = 0; v-y (independently selected) = 0 or 1; R = linker-anti-TNF IG chimera protein.

FIG. 38W



$$\mathbf{B} \leftarrow \begin{pmatrix} (\mathrm{Sia})_{b} \\ -\mathrm{GalNAc-(Gal)}_{a} - (\mathrm{Sia})_{c} - (\mathrm{R})_{d} \end{pmatrix}_{e}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = modifying group, mannose, oligomannose.

FIG. 39A

CHO, BHK, 293 cells, Vero expressed IL-2 a-c, e (independently selected) = 0 or 1; d = 0

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 39B

Insect cell expressed IL-2 a, e (independently selected) = 0 or 1; b, c, d = 0.

- 1. Galactosyltransferase, UDP-Gal
- 2. CMP-SA-PEG, ST3Gal1

a, c, d, e (independently selected) = 0 or 1; R = PEG.

E. coli expressed IL-2 a-e=0.

- 1. GalNAc Transferase, UDP-GalNAc
- 2. CMP-SA-PEG, sialyltransferase

c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

FIG. 39D

NSO expressed IL-2 a, e (independently selected) = 0 or 1; b, c, d = 0

- 1. CMP-SA-levulinate, ST3Gal1
- $2. H_4N_2$ -PEG

a, c, d, e (independently selected) = 0 or 1; b = 0; R = PEG.

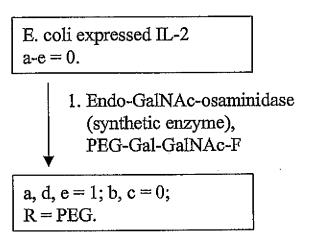


FIG. 39F

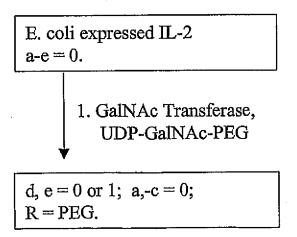


FIG. 39G

2 peptides

A and A' - N-linked sites

B - O-linked sites

$$\mathbf{A} = (\operatorname{Gal}_{a})_{e} - (\operatorname{Sia})_{f} - (\operatorname{Ria})_{g} - (\operatorname{Ria})$$

$$\mathbf{B}$$
 \leftarrow $\left(\begin{array}{c} (\mathrm{Sia})_{o} \\ -\mathrm{GalNAc-(Gal)}_{n}-(\mathrm{Sia})_{p}-(\mathrm{R})_{z} \end{array}\right)_{c}$

a-d, i, n-u (independently selected) = 0 or 1.
aa, bb (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 20.
v-z = 0; R = polymer, glycoconjugate.

FIG. 40A

```
CHO, BHK, 293s cells, Vero, MDCK, HEKC expressed Factor VIII.

e-h = 1 to 4;

aa, bb, a-d, j-m, i, n-u (independently selected) = 0 or 1;

v-z = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3

```
e-h = 1 to 4;
aa, bb, a-d, i, n, q-u (independently selected) = 0 or 1;
o, p, z = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 40B

```
CHO, BHK, 293S cells, Vero, MDCK, 293S, HEKC expressed Factor VIII.

e-h = 1 to 4;

aa, bb, a-d, j-m, i, n-u (independently selected) = 0 or 1;

v-z = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3
- 3. ST3Gal1, CMP-SA

```
e-h = 1 to 4;
aa, bb, a-d, i, n, p-u (independently selected) = 0 or 1;
o, z = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 40C

```
CHO, BHK, 293s cells, Vero, MDCK, HEKC expressed Factor VIII.

e-h = 1 to 4;

aa, bb, a-d, j-m, i, n-u (independently selected)=0 or 1;

v-z = 0.
```

1. CMP-SA-PEG, ST3Gal3

```
e-h = 1 to 4;
aa, bb, a-d, i, n-u (independently selected) = 0 or 1;
z = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 40D

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.

e-h = 1 to 4;

aa, bb, a-d, j-m, i, n-u (independently selected) 0 or 1;

v-z = 0.
```

1. CMP-SA-PEG, ST3Gal1

```
e-h = 1 to 4;
aa, bb, a-d, i, n-u (independently selected) = 0 or 1;
z = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 40E

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, a-d, j-m, i, n-u (independently selected)=0 or 1;
v-z = 0.
```

1. CMP-SA-PEG, α 2,8-ST

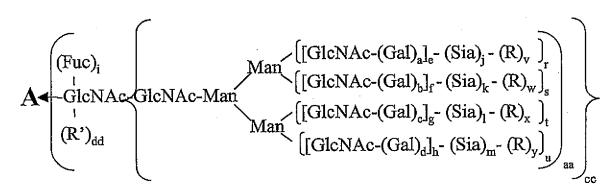
```
e-h = 1 to 4;
aa, bb, a-d, i, n-y (independently selected) = 0 or 1;
z = 0; j-m (independently selected) = 0 to 2;
v-y (independently selected) = 1,
when j-m (independently selected) is 2;
R = PEG.
```

FIG. 40F

2 peptides

A or A' - N-linked sites

B - O-linked sites



$$\mathbf{B} \leftarrow \begin{pmatrix} (\mathrm{Sia})_{o} \\ -\mathrm{GalNAc-(Gal)}_{n} - (\mathrm{Sia})_{p} - (\mathrm{R})_{z} \end{pmatrix}_{q}$$

Alternate structure for some N-linked structures of A.

a-d, i, n-u, (independently selected) = 0 or 1.
aa, bb, cc, dd (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 20.
v-z = 0;
R = modifying group, mannose, oligo-mannose.
R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 40G

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.

e-h = 1 to 4;

aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;

dd, v-z = 0.
```

1. CMP-SA-levulinate, ST3Gal3,
 2. H₄N₂-PEG

```
e-h = 1 to 4;
aa, bb, cc, a-d, i, n-u (independently selected) = 0 or 1;
dd, z = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 40H

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.

e-h = 1 to 4;

aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;

dd, v-z = 0.
```

endo-H
 galactosyltransferase, UDP-Gal-PEG

```
e-h = 1 to 4;
aa, bb, dd, a-d, i, j-u (independently selected) = 0 or 1;
cc, v-z = 0; R' = -Gal-PEG.
```

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;
dd, v-z = 0.
```

- 1. ST3Gal3, CMP-SA
- 2. endo-H
- 3. galactosyltransferase, UDP-Gal-PEG

```
e-h = 1 to 4;
aa, bb, dd, a-d, i, j-u (independently selected) = 0 or 1;
cc, v-z = 0; R' = -Gal-PEG.
```

FIG. 40J

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.

e-h = 1 to 4;

aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;

dd, v-z = 0.
```

- 1. mannosidases
- 2. GNT 1 & 2, UDP-GlcNAc
- 3. galactosyltransferase, UDP-Gal-PEG

```
e-h = 1 to 4;
aa, a-d, i, j-y (independently selected) = 0 or 1;
bb, cc, dd, z = 0; R = PEG.
```

FIG. 40K

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.

e-h = 1 to 4;

aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;

dd, v-z = 0.
```

- 1. mannosidases
- 2. GNT-1,2, 4 & 5; UDP-GlcNAc
- 3. galactosyltransferase, UDP-Gal
- 4. ST3Gal3, CMP-SA

```
e-h = 1 to 4;
aa, bb, cc, a-d, i, j-q (independently selected) = 0 or 1;
dd, v-z=0.
```

FIG. 40L

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.

e-h = 1 to 4;

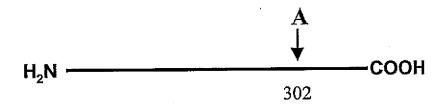
aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;

dd, v-z = 0.
```

mannosidases
 GNT-1, UDP-GlcNAc-PEG

```
e-h = 0 to 4;
aa, a-d, i, j-y (independently selected) = 0 or 1;
bb, cc, dd, z = 0.
```

FIG. 40M



$$\mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_{a}]_{e} - (\mathrm{Sia})_{j} - (\mathrm{R})_{v} \end{bmatrix}_{r} \\ - (\mathrm{GlcNAc} - \mathrm{GlcNAc} - \mathrm{Man} \\ - (\mathrm{GlcNAc} - (\mathrm{Gal})_{b}]_{f} - (\mathrm{Sia})_{k} - (\mathrm{R})_{w} \end{bmatrix}_{s} \\ - (\mathrm{GlcNAc} - (\mathrm{Gal})_{b}]_{f} - (\mathrm{Sia})_{l} - (\mathrm{R})_{x} \end{bmatrix}_{t} \\ - (\mathrm{GlcNAc} - (\mathrm{Gal})_{d}]_{h} - (\mathrm{Sia})_{m} - (\mathrm{R})_{y} \end{bmatrix}_{u}$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

CHO, BHK, 293 cells, Vero expressed Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 41B

```
CHO, BHK, 293 cells, Vero expressed Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 41C

```
NSO expressed Urokinase.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0;

Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and α-galactosidase
- 2. α-Galactosyltransferase, UDP-Gal
- ▼ 3. CMP-SA-PEG, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 41D

```
CHO, BHK, 293 cells, Vero expressed Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- 1. Sialidase
- CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 41E

```
CHO, BHK, 293 cells, Vero expressed Urokinase.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

 CMP-SA-levulinate, ST3Gal3, buffer, salt
 H₄N₂-PEG

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 41F

```
CHO, BHK, 293 cells, Vero expressed Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

1. CMP-SA, α2,8-ST

```
a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1;
j-m (independently selected) = 0-20;
v-y (independently selected) = 0.
```

FIG. 41G



$$\mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc-(Gal)_a}]_e - (\mathrm{Sia})_j - (\mathrm{R})_v \end{bmatrix}_r \\ [\mathrm{GlcNAc-(Gal)_b}]_f - (\mathrm{Sia})_k - (\mathrm{R})_w \end{bmatrix}_s \\ [\mathrm{GlcNAc-(Gal)_b}]_g - (\mathrm{Sia})_l - (\mathrm{R})_x \end{bmatrix}_t \\ [\mathrm{GlcNAc-(Gal)_b}]_g - (\mathrm{Sia})_l - (\mathrm{R})_x \end{bmatrix}_t \\ [\mathrm{GlcNAc-(Gal)_d}]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u = 0$$

a-d, i, n, p-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0;
R = modifying group, mannose, oligo-mannose;
R' = H, glycosyl residue, modifying group,
glycoconjugate.

FIG. 41H

```
Insect cell expressed Urokinase.
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1;
j-n = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 411

```
Yeast expressed Urokinase.

a-n=0;
q-y (independently selected) = 0 to 1;
p=1; R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

```
a-m, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.
```

FIG. 41J

```
CHO, BHK, 293 cells, Vero expressed Urokinase.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; n, v-y = 0.
```

- 1. CMP-SA-linker-SA-CMP, ST3Gal3
- 2. ST3Gal1, desialylated Urokinase produced in CHO.
- 3. CMP-SA, ST3Gal3, ST3Gal1

```
a-m, q-u (independently selected) = 0 or 1;

p = 1; n = 0;

v-y (independently selected) = 0 or 1;

R = linker-Urokinase.
```

FIG. 41K

```
Isolated Urokinase.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0; n = 0;
Sia (independently selected) = Sia or SO<sub>4</sub>;
Gal (independently selected) = Gal or GalNAc;
GlcNAc (independently selected) = GlcNAc or GlcNAc-Fuc.
```

1. sulfohydrolase

2. CMP-SA-PEG, sialyltransferase

```
a-d, i-m, q-u (independently selected) = 0 or 1;

n = 0; e-h = 1; Sia = Sia;

Gal (independently selected) = Gal or GalNAc;

GlcNAc (independently selected) = GlcNAc or GlcNAc-Fuc.

v-y (independently selected) = 0 or 1;

R = PEG.
```

FIG. 41L

```
Isolated Urokinase.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; n = 0; v-y = 0;

Sia (independently selected) = Sia or SO<sub>4</sub>;

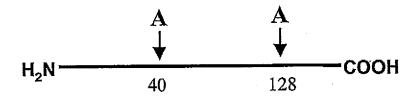
Gal (independently selected) = Gal or GalNAc;

GlcNAc (independently selected) = GlcNAc or GlcNAc-Fuc.
```

- 1. sulfohydrolase, hexosaminidase
- 2. UDP-Gal-PEG, galactosyltransferase

```
a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1; j-n = 0; Gal (independently selected) = Gal;
GlcNAc (independently selected) = GlcNAc or GlcNAc-Fuc;
v-y (independently selected) = 0 or 1; R = PEG.
```

FIG. 41M



$$\mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc\text{-}(Gal)}_a]_e - (\mathrm{Sia})_j - (\mathrm{R})_v \end{bmatrix}_r^r \\ - \mathrm{GlcNAc\text{-}GlcNAc\text{-}Man} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc\text{-}(Gal)}_b]_f - (\mathrm{Sia})_k - (\mathrm{R})_w \end{bmatrix}_s^r \\ - \mathrm{GlcNAc\text{-}GlcNAc\text{-}Man} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc\text{-}(Gal)}_c]_g - (\mathrm{Sia})_l - (\mathrm{R})_x \end{bmatrix}_t^r \\ - \mathrm{GlcNAc\text{-}(Gal)}_d \end{bmatrix}_h^r - (\mathrm{Sia})_m^r - (\mathrm{R})_y \end{bmatrix}_u^q$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer, glycoconjugate.

FIG. 42A

```
CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- 1. Sialidase
 - 2. CMP-SA-PEG (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 42B

```
CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 42C

```
NSO expressed DNase I.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0;

Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and α-galactosidase
- 2. α-Galactosyltransferase, UDP-Gal
- **★** 3. CMP-SA-PEG, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 42D

```
CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

 CMP-SA-levulinate, ST3Gal3, buffer, salt
 H₄N₂-PEG

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

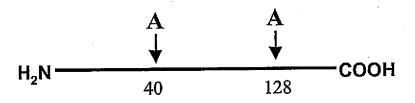
FIG. 42F

CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1;
j-m (independently selected) = 0-20;
v-y (independently selected) = 0.

FIG. 42G



$$\mathbf{A} \leftarrow \begin{bmatrix} \left[\operatorname{GlcNAc-(Gal)}_{a} \right]_{e^{-}} \left(\operatorname{Sia} \right)_{j^{-}} \left(\operatorname{R} \right)_{v} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{b} \right]_{f^{-}} \left(\operatorname{Sia} \right)_{k^{-}} \left(\operatorname{R} \right)_{w} \right]_{g} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{b} \right]_{g^{-}} \left(\operatorname{Sia} \right)_{l^{-}} \left(\operatorname{R} \right)_{x} \right]_{l} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\operatorname{GlcNAc-(Gal)}_{d^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\operatorname{GlcNAc-(Gal)}_{d^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\operatorname{GlcNAc-(Gal)}_{d^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \\ \left[\operatorname{GlcNAc-(Gal)}_{d^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \\ \left[\operatorname{GlcNAc-(Gal)}_{d^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \\ \left[\operatorname{GlcNAc-(Gal)}_{d^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname$$

a-d, i, n, p-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0;
R = modifying group, mannose, oligo-mannose;
R' = H, glycosyl residue, modifying group,
glycoconjugate.

FIG. 42H

```
Insect cell expressed DNase I.
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1; j-n = 0;
v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 421

```
Yeast expressed DNase I.

a-n = 0;

q-y (independently selected) = 0 to 1;

p = 1; R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

a-n, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.

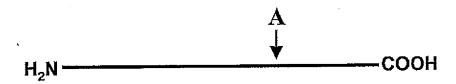
FIG. 42J

```
CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; n, v-y=0.
```

- 1. CMP-SA-linker-SA-CMP, ST3Gal3
- 2. ST3Gal1, desialylated alpha-1-Proteinase inhibitor.
- 3. CMP-SA, ST3Gal3, ST3Gal1

```
a-m, q-u (independently selected) = 0 or 1;
p = 1; n = 0;
v-y (independently selected) = 0 or 1;
R = linker- alpha-1-Proteinase inhibitor.
```

FIG. 42K



$$\begin{array}{c} \text{(Fuc)}_{i} \\ \textbf{A} \leftarrow \text{-GlcNAc--Gal)}_{i} \\ \textbf{(R')}_{n} \end{array} \qquad \begin{array}{c} \text{Man} \left[\left[\text{GlcNAc--(Gal)}_{a} \right]_{e} - \left(\text{Sia} \right)_{j} - \left(\text{R} \right)_{v} \right]_{r} \\ \left[\left[\text{GlcNAc--(Gal)}_{b} \right]_{f} - \left(\text{Sia} \right)_{k} - \left(\text{R} \right)_{w} \right]_{s} \\ \left[\left[\text{GlcNAc--(Gal)}_{c} \right]_{g} - \left(\text{Sia} \right)_{l} - \left(\text{R} \right)_{x} \right]_{t} \\ \left[\left[\text{GlcNAc--(Gal)}_{d} \right]_{h} - \left(\text{Sia} \right)_{m} - \left(\text{R} \right)_{y} \right]_{u} \\ z \end{array}$$

a-d, i, r-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y = 0; z = 0 or 1; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 43A

```
CHO, BHK, 293 cells, Vero expressed Insulin. a-m, r-u (independently selected) = 0 or 1; n = 0; v-y = 0; z = 1.
```

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3

```
a-m, r-u (independently selected) = 0 or 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
n = 0; R = PEG; z = 1.
```

FIG. 43B

```
Insect cell expressed Insulin.
a-h, j-n, s-y = 0;
i, r (independently selected) = 0 or 1; z = 1.
```

1. GNT's 1&2, UDP-GlcNAc-PEG

```
a-d, f, h, j-n, s, u, w, y = 0;
e, g, i, r, t, v, x (independently selected) = 0 or 1;
v, x (independently selected) = 1,
when e, g (independently selected) is 1;
z = 1; R = PEG.
```

FIG. 43C

Yeast expressed Insulin.

a-n = 0; r-y (independently selected) = 0 to 1;

z=1;

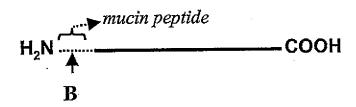
R (branched or linear) = Man, oligomannose or polysaccharide.

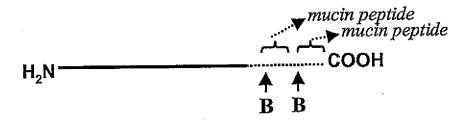
- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal-PEG

a-m, r-z= 0; n = 1; R' = -Gal-PEG.

FIG. 43D







$$\mathbf{B} \leftarrow \begin{bmatrix} (\mathrm{Sia})_{b} \\ -\mathrm{GalNAc-(Gal)}_{a} - (\mathrm{Sia})_{c} - (\mathrm{R})_{d} \end{bmatrix}_{e}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = polymer

FIG. 43E

CHO, BHK, 293 cells, Vero expressed insulinmucin fusion protein. a-c, e (independently selected) = 0 or 1; d = 0

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 43F

Insect cell expressed Insulin-mucin fusion protein. a, e (independently selected) = 0 or 1; b, c, d = 0.

1. Galactosyltransferase, UDP-Gal-PEG

a, d, e (independently selected) = 0 or 1; b, c = 0; R = PEG.

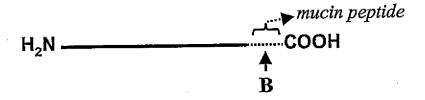
FIG. 43G

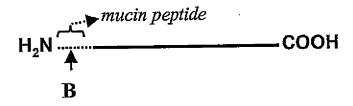
E. coli expressed Insulin-mucin fusion protein. a-e=0.

- 1. GalNAc Transferase, UDP-GalNAc
- 2. CMP-SA-PEG, sialyltransferase

c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

FIG. 43H





$$\mathbf{B} \leftarrow \begin{pmatrix} (\operatorname{Sia})_{b} \\ -\operatorname{GalNAc-(Gal)}_{a} - (\operatorname{Sia})_{c} - (R)_{d} \end{pmatrix}_{e}$$

a-c, e (independently selected) = 0 or 1; d=0; R = modifying group, mannose, oligo-mannose.

FIG. 431

E. coli expressed Insulin-mucin fusion protein. a-e, n = 0.

 GalNAc Transferase, UDP-GalNAc-PEG

d, e (independently selected) = 0 or 1; a-c, n = 0; R = PEG.

FIG. 43J

E. coli expressed Insulin-mucin fusion protein. a-e, n = 0.

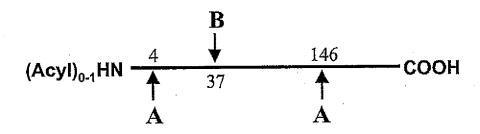
- GalNAc Transferase,
 UDP-GalNAc-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
- 3. CMP-SA, ST3Gal3

d, e (independently selected) = 0 or 1; a-c, n = 0; R = linker-transferrin.

E. coli expressed Insulin (N)—no mucin peptide. a-e, n = 0.

- 1. NHS-CO-linker-SA-CMP
- ST3Gal3, asialo-transferrin
 CMP-SA, ST3Gal3

FIG. 43L



$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} & \operatorname{Man} & [(\operatorname{GlcNAc-(Gal)}_{a}]_{e^{-}} (\operatorname{Sia})_{j^{-}} (R)_{v} \\ -\operatorname{GlcNAc-GlcNAc-Man} & \operatorname{Man} & [(\operatorname{GlcNAc-(Gal)}_{b}]_{f^{-}} (\operatorname{Sia})_{k^{-}} (R)_{w}]_{s} \\ -\operatorname{GlcNAc-(Gal)}_{o}]_{g^{-}} & (\operatorname{Sia})_{l^{-}} (R)_{x} \\ & [(\operatorname{GlcNAc-(Gal)}_{d}]_{h^{-}} (\operatorname{Sia})_{m^{-}} (R)_{y}]_{u} \\ & \\ \mathbf{B} \leftarrow \begin{bmatrix} (\operatorname{Sia})_{o} \\ -\operatorname{GalNAc-(Gal)}_{n^{-}} (\operatorname{Sia})_{p^{-}} (R)_{z} \\ -\operatorname{GalNAc-(Gal)}_{n^{-}} (R)_{z} \\ -\operatorname{G$$

a-d, i, n-u, aa (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer, glycoconjugate.

FIG. 44A

CHO, BHK, 293 cells, Vero expressed M-antigen. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.

- 1. Sialidase
- 2. CMP-SA-linker-lipid-A, ST3Gal3

```
a-d, i-m, q-u, aa (independently selected) = 0 or 1;
o, p, z = 0; n, e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = linker-lipid-A.
```

FIG. 44B

```
CHO, BHK, 293 cells, Vero expressed M-antigen. a-d, i-m, o-u, as (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.
```

- 1. sialidase
- 2. CMP-SA-linker-tetanus toxin, ST3Gal1
- 3. CMP-SA, ST3Gal3

a-d, i-m, p-u, z, aa (independently selected) = 0 or 1; o, v-y = 0; n, e-h = 1; R = tetanus toxin.

```
NSO expressed M-antigen.
a-d, i-n, o-u, aa (independently selected) = 0 or 1;
e-h = 1; v-z = 0;
Sia (independently selected) = Sia or Gal.
```

- 1. α-galactosidase
- 2. CMP-SA, ST3Gal3
- 2. CMP-SA-KLH, ST3Gal1

```
a-d, i-n, p-u, z, aa (independently selected) = 0 or 1;
e-h = 1; o, v-y = 0;
z = 1, when p = 1;
R = KLH.
```

FIG. 44D

```
Yeast expressed M-antigen.
a-p, z = 0; q-y, aa (independently selected) = 0 to 1;
R (branched or linear) = Man, oligomannose;
GalNAc = Man.
```

α1,2-mannosidase
 GNT 1,
 UDP-GlcNAc-linker-diphtheria toxin.

e, q, 1, m, r, t, u, v, aa (independently selected) =0 or 1; a-d, f-h, j, k, n-p, s, w-z = 0; Sia = Man; R = linker-diphtheria toxin.

FIG. 44E

CHO, BHK, 293 cells, Vero expressed M-antigen. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.

- 1. CMP-SA-levulinate, ST3Gal3,
- 2. H₄N₂-linker-DNA

a-d, i-m, o-y, aa (independently selected) = 0 or 1; z = 0; n, e-h = 1; R = linker-DNA.

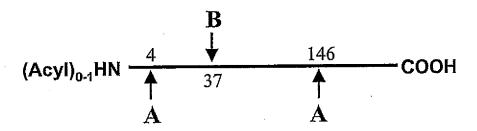
FIG. 44F

CHO, BHK, 293 cells, Vero expressed M-antigen. a-d, i-n, o-u, as (independently selected) = 0 or 1; e-h=1; v-z=0.

1. CMP-SA, poly- α 2,8-ST

a-d, i, n-u, aa (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-100; v-z (independently selected) = 0.

FIG. 44G



$$\mathbf{A} \leftarrow \underbrace{ \begin{array}{c} (\operatorname{Fuc})_{i} \\ -\operatorname{GlcNAc-GlcNAc-Man} \\ | (R')_{cc} \end{array}}_{\text{Man}} \underbrace{ \begin{array}{c} [\operatorname{GlcNAc-(Gal)}_{a}]_{e^{-}} (\operatorname{Sia})_{j} - (R)_{v} \\ [\operatorname{GlcNAc-(Gal)}_{b}]_{f^{-}} (\operatorname{Sia})_{k} - (R)_{w} \\ | (\operatorname{GlcNAc-(Gal)}_{c}]_{g^{-}} (\operatorname{Sia})_{i} - (R)_{x} \\ | (\operatorname{GlcNAc-(Gal)}_{d}]_{h^{-}} (\operatorname{Sia})_{m^{-}} (R)_{y} \\ | (\operatorname{GlcNAc-(Gal)}_{d})_{h^{-}} (\operatorname{Gal})_{h^{-}} (R)_{y} \\ | (\operatorname{GlcNAc-(Gal)}_{d})_{h^{-}} (R)_{y} \\ | (\operatorname{G$$

$$\mathbf{B}$$

$$(Sia)_{o}$$

$$-GalNAc-(Gal)_{n}-(Sia)_{p}-(R)_{z}$$
_{aa}

a-d, i, n, q-u, aa, bb, (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-p (independently selected) = 0 to 100. Cc, v-y = 0; R = modifying group, mannose, oligo-mannose. R'= H, glycosyl residue, modifying group, glycoconjugate.

FIG. 44H

```
Insect cell expressed M-antigen.
a-d, f, h, j-m, o, p, s, u, v-z, cc = 0;
bb = 1;
e, g, i, n, q, r, t, aa (independently selected) = 0 or 1.
```

 GNT-2, UDP-GlcNAc-linker-Neisseria protein

```
a, c, e, g, i, n, q, r, t, v, x, aa (independently selected) = 0 or 1;
b, d, f, h, j-p, s, u, w, y, z, cc = 0;
bb = 1; R = -linker-Neisseria protein.
```

FIG. 441

```
Yeast expressed M-antigen.

a-p, z, cc = 0;

q-y, aa (independently selected) = 0 to 1;

bb = 1; R (branched or linear) = Man, oligomannose;

GalNAc = Man.
```

1. Endoglycanase

2. Galactosyltransferase, UDP-Gal-linker-Neisseria protein

```
a-p, r-z, bb = 0;
q, aa, cc (independently selected) = 0 or 1;
R' = -Gal-linker-Neisseria protein.
```

FIG. 44J

```
Yeast expressed M-antigen.

a-p, z, cc = 0;

q-y, aa (independently selected) = 0 to 1; bb = 1;

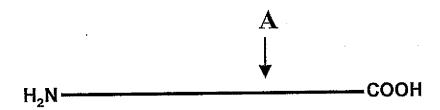
R (branched or linear) = Man, oligomannose;

GalNAc = Man.
```

- 1. mannosidases
- 2. GNT 1 & 2, UDP-GlcNAc
- 3. UDP-Gal, Galactosyltransferase,
- 4. CMP-SA, sialyltransferase

a, c, e, g, j, l, q, r, t, aa (independently selected) = 0 or 1; b, d, f, h, k, m-p, s, u-z, cc = 0; bb = 1.

FIG. 44K



$$\begin{array}{c} \text{(Fuc)}_{i} \\ \text{A} \leftarrow \text{-GlcNAc-Man} \\ \text{(R')}_{n} \end{array} \\ \text{Man} \begin{array}{c} \left[\left[\text{GlcNAc-(Gal)}_{a} \right]_{e^{-}} \left(\text{Sia)}_{j^{-}} \left(\text{R)}_{v^{-}} \right)_{r} \\ \left[\left[\text{GlcNAc-(Gal)}_{b} \right]_{f^{-}} \left(\text{Sia)}_{k^{-}} \left(\text{R} \right)_{w} \right)_{s} \\ \text{Man} \end{array} \\ \begin{array}{c} \left[\left[\text{GlcNAc-(Gal)}_{c} \right]_{g^{-}} \left(\text{Sia)}_{l^{-}} \left(\text{R} \right)_{x} \right)_{t} \\ \left[\left[\text{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\text{Sia)}_{m^{-}} \left(\text{R} \right)_{y} \right)_{u} \end{array} \right]_{z} \end{array}$$

a-d, i, r-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y = 0; z = 0 or 1; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

CHO, BHK, 293 cells, Vero expressed Growth Hormone.

```
a-m, r-u (independently selected) = 0 or 1;
 n = 0; v-y = 0; z = 1.
```

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3

a-m, r-u (independently selected) = 0 or 1; v-y (independently selected) = 1, when j-m (independently selected) is 1; n = 0; R = PEG; z = 1.

FIG. 45B

WO 03/031464

```
Insect cell expressed growth hormone.
a-h, j-n, s-y = 0;
i, r (independently selected) = 0 or 1; z = 1.
```

1. GNT's 1&2, UDP-GlcNAc-PEG

```
a-d, f, h, j-n, s, u, w, y = 0;
e, g, i, r, t, v, x (independently selected)= 0 or 1;
v, x (independently selected) = 1,
when e, g (independently selected) is 1;
z = 1; R = PEG.
```

FIG. 45C

Yeast expressed growth hormone.

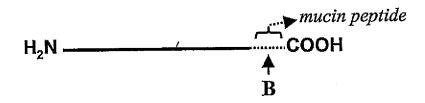
a-n=0; r-y (independently selected) = 0 to 1;

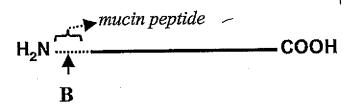
R (branched or linear) = Man, oligomannose or polysaccharide.

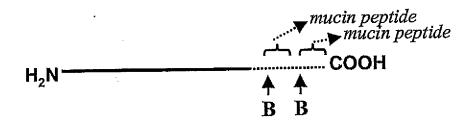
- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal-PEG

a-m, r-z= 0; n = 1; R' = -Gal-PEG.

FIG. 45D







$$\mathbf{B} \leftarrow \begin{bmatrix} (\mathrm{Sia})_{b} \\ -\mathrm{GalNAc-(Gal)}_{a} - (\mathrm{Sia})_{c} - (\mathrm{R})_{d} \end{bmatrix}_{e}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = modifying group, mannose, oligomannose.

FIG. 45E

CHO, BHK, 293 cells, Vero expressed growth hormone-mucin fusion protein. a-c, e (independently selected) = 0 or 1; d = 0

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 45F

Insect cell expressed Growth Hormone-mucin fusion protein.

a, e (independently selected) = 0 or 1; b, c, d = 0.

1. Galactosyltransferase, UDP-Gal-PEG

a, d, e (independently selected) = 0 or 1; b, c = 0; R = PEG.

FIG. 45G

E. coli expressed growth hormone-mucin fusion protein.

a-e=0.

- 1. GalNAc Transferase, UDP-GalNAc
- 2. CMP-SA-PEG, sialyltransferase

c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

FIG. 45H

E. coli expressed growth hormone-mucin fusion protein.

a-e, n = 0.

1. GalNAc Transferase, UDP-GalNAc-PEG

d, e (independently selected) = 0 or 1; a-c, n = 0; R = PEG.

FIG. 451

E. coli expressed growth hormone-mucin fusion protein.

a-e, n = 0.

- GalNAc Transferase, UDP-GalNAc-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
- ★ 3. CMP-SA, ST3Ga13

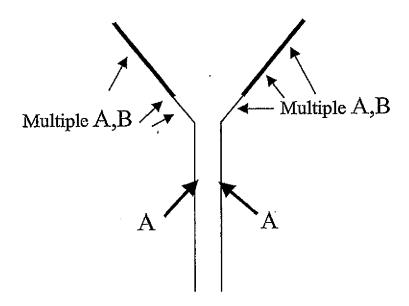
d, e (independently selected) = 0 or 1; a-c, n = 0; R = linker-transferrin.

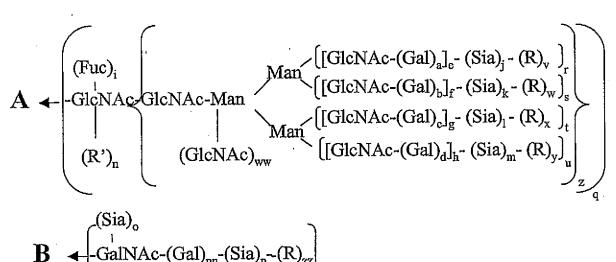
FIG. 45J

E. coli expressed growth hormone (N)—no mucin peptide. a-e, n = 0.

- 1. NHS-CO-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
- 3. CMP-SA, ST3Gal3

a-e=0; n=1; R'=linker-transferrin.





a-d, i-m, q-u, w, z, nn, ww, zz (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4.

n, v-y = 0;

R = modifying group, mannose, oligo-mannose;

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 46A

CHO, BHK, 293 cells, Vero or transgenic animals expressed TNF Receptor IgG Fusion. a-m, o-u, aa (independently selected) = 0 or 1; n = 1; v-z = 0.

- 1. CMP-SA, ST3Gal1
- 2. galactosyltransferase, UPD-Gal
- 3. CMP-SA-PEG, ST3Gal3

a-m, o-u, v-y, aa (independently selected) = 0 or 1; n = 1; z = 0; R = PEG.

FIG. 46B

CHO, BHK, 293 cells, Vero expressed TNF Receptor IgG Fusion.
a-m, o-u, aa (independently selected) = 0 or 1; n = 1; v-z = 0.

1. sialidase ▼ 2. CMP-SA-PEG, ST3Gal1

a-i, p-u, z, aa (independently selected) = 0 or 1; n = 1; o, j-m, v-y=0; R=PEG.

FIG. 46C

CHO, BHK, 293 cells, Vero expressed TNF Receptor IgG Fusion.
a-m, o-u, aa (independently selected) = 0 or 1; n = 1; v-z = 0.

1. galactosyltransferase, UPD-Gal-PEG

a-m, o-u, v-y, as (independently selected) = 0 or 1; n = 1; z = 0; R = PEG.

FIG. 46D

CHO, BHK, 293 cells, Vero or transgenic animals expressed TNF Receptor IgG Fusion. a-m, o-u, aa (independently selected) = 0 or 1; n = 1; v-z = 0.

1. CMP-SA, ST3Gal12. galactosyltransferase, UPD-Gal-PEG

a-m, o-u, v-y, as (independently selected) = 0 or 1; n = 1; z = 0; R = PEG.

FIG. 46E

CHO, BHK, 293 cells, Vero or transgenic animals expressed TNF Receptor IgG Fusion. a-m, o-u, as (independently selected) = 0 or 1; n = 1; v-z = 0.

1. CMP-SA-levulinate, ST3Gal1
2. H₄N₂-PEG

a-m, o-u, v-y, as (independently selected) = 0 or 1; n = 1; z = 0; R = PEG.

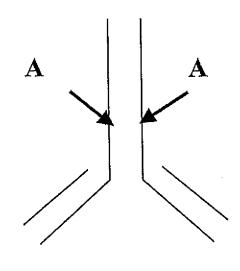
FIG. 46F

CHO, BHK, 293 cells, Vero expressed
TNF Receptor IgG Fusion.
a-m, o-u, aa (independently selected) = 0 or 1;
n = 1; v-z = 0.

1. CMP-SA-PEG, α2,8-ST

a-i, o, q-u, v-z, aa (independently selected) = 0 or 1;
n = 1; j-m, p (independently selected) = 0 to 2;
v-z (independently selected) = 1,
when j-m, p (independently selected) is 2;
R = PEG.

FIG. 46G



$$\begin{array}{c} \text{(Fuc)}_{i} \\ \text{(GlcNAc-(Gal)}_{a}]_{e}\text{-} (Sia)_{j}\text{-} (R)_{v} \\ \text{([GlcNAc-(Gal)}_{b}]_{f}\text{-} (Sia)_{k}\text{-} (R)_{w} \\ \text{(R')}_{n} \\ \text{(GlcNAc-(Gal)}_{d}]_{h}\text{-} (Sia)_{m}\text{-} (R)_{y} \\ \text{(GlcNAc-(Gal)}_{d}]_{h}\text{-} (Sia)_{m}\text{-} (R)_{w} \\ \text{(GlcNAc-(Gal)}_{d})_{m}\text{-} (R)_{w} \\ \text{(GlcNAc-(Gal)}_{d})_{m}\text{-} (R)_{w} \\ \text{(GlcNAc-(Gal)}_{d})_{m}\text{-} (R)_{w} \\ \text{(GlcNAc-(Gal)}_{d})_{m}\text{-} (R)_{w} \\ \text{(GlcNAc-(Gal)}_{d})_{m} \\ \text{(GlcNAc-(Gal)}_{d})_{m}\text{-} (R)_{w} \\$$

a-d, i, l, q-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4.

j-k (independently selected) = 0 or 1.

M = 0 to 20.

n, v-y=0; z=0 or 1;

R = polymer, toxin, radioisotope-complex, drug, mannose, oligo-mannose.

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 47A

```
CHO, BHK, 293 cells, Vero expressed Herceptin.
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y=0;
q, z=1.
```

- 1. galactosyltransferase, UPD-Gal
- 2. CMP-SA-toxin, ST3Gal3

```
a, c, i, j, l (independently selected) = 0 or 1;
e, g, r, t = 1; R = toxin;
f, h, k, m, n, s, u-y = 0; q, z = 1;
v-y (independently selected) = 51,
when j, l (independently selected) is 1.
```

FIG. 47B

```
CHO, BHK, 293 cells, Vero or fungal expressed Herceptin.

a, c, i (independently selected) = 0 or 1;

e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;

q, z = 1.
```

1. galactosyltransferase, UPD-Gal-Toxin

```
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, j-m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = toxin.
```

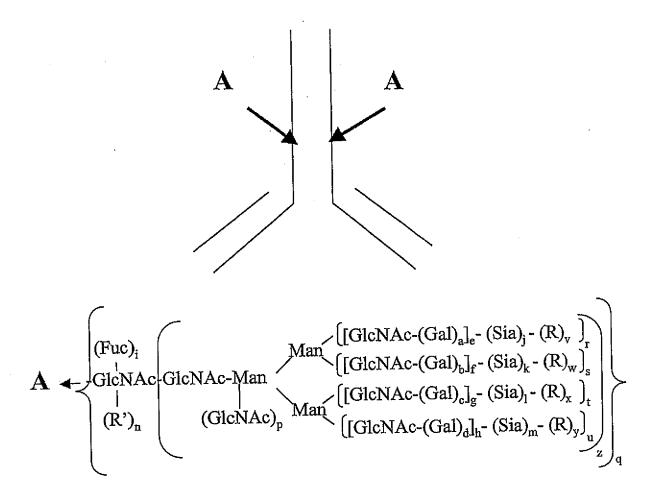
FIG. 47C

Fungi expressed Herceptin. e, g, i, r, t (independently selected) = 0 or 1; a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal
- 3.. CMP-SA-radioisotope complex, ST3Gal3

a-m, r-z= 0; q, n = 1; R' = -Gal-Sia-radioisotope complex.

FIG. 47D



a-d, i, p-u, (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-m (independently selected) = 0 or 1.
n, v-y = 0; z = 0 or 1;
R = polymer, toxin, radioisotope-complex, drug, mannose, oligo-mannose.
R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 48A

```
CHO, BHK, 293 cells, Vero expressed Synagis.

a, c, i (independently selected) = 0 or 1;

e, g, r, t = 1;

b, d, f, h, j-m, n, s, u-y = 0; q, z = 1.
```

1. galactosyltransferase, UPD-Gal

2. CMP-SA-PEG, ST3Gal3

```
a, c, i, j, w, (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, k, m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when j, 1 (independently selected) is 1;
R = PEG.
```

FIG. 48B

```
CHO, BHK, 293 cells, Vero or fungal expressed Synagis.

a, c, i (independently selected) = 0 or 1;

e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;

q, z = 1.
```

 galactosyltransferase, UPD-Gal-PEG

```
a, c, i, w (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, j-m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = PEG.
```

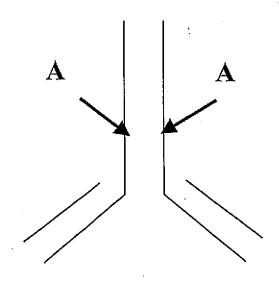
FIG. 48C

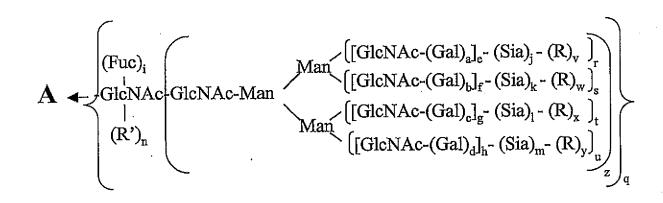
Fungi expressed Synagis. e, g, i, r, t (independently selected) = 0 or 1; a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.

- 1. Endo-H
- Galactosyltransferase, UDP-Gal
 CMP-SA-PEG, ST3Gal3

a-m, r-z=0; q, n=1; R'=-Gal-Sia-PEG.

FIG. 48D





a-d, i, q-u, w (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 6.

j-m (independently selected) = 0 to 20.

n, y-y=0; z=0 or 1;

R = polymer, toxin, radioisotope-complex, drug, mannose, oligo-mannose.

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 49A

```
CHO, BHK, 293 cells, Vero expressed Remicade.
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;
q, z = 1.
```

- 1. galactosyltransferase, UPD-Gal
- 2. CMP-SA-PEG, ST3Gal3

```
a, c, i, j, 1 (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, k, m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when j, 1 (independently selected) is 1;
R = PEG.
```

FIG. 49B

```
CHO, BHK, 293 cells, Vero or fungal expressed Remicade.

a, c, i (independently selected) = 0 or 1;

e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;

q, z = 1.
```

1. galactosyltransferase, UPD-Gal-PEG

```
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, j-m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = PEG.
```

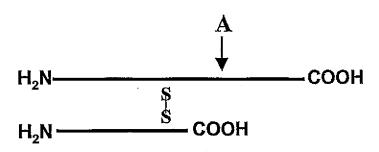
FIG. 49C

```
Fungi expressed Remicade.
e, g, i, r, t (independently selected) = 0 or 1;
a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.
```

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal
- 3.. CMP-SA-radioisotope complex, ST3Gal3

a-m, r-z= 0; q, n = 1; R' = -Gal-Sia-radioisotope complex.

FIG. 49D



$$\mathbf{A} \leftarrow \begin{array}{c} \text{(Fuc)}_{i} \\ \text{(GlcNAc-(Gal)}_{a}]_{e^{-}} \text{(Sia)}_{j^{-}} \text{(R)}_{v} \\ \text{[GlcNAc-(Gal)}_{b}]_{f^{-}} \text{(Sia)}_{k^{-}} \text{(R)}_{w} \\ \text{(R')}_{n} \\ \text{(R')}_{n} \end{array}$$

a-d, i, q-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-m (independently selected) = 0 or 1.
n, v-y = 0; z = 0 or 1;
R = modifying group, mannose, oligo-mannose;
R' = H, glycosyl residue, modifying group,
glycoconjugate.

FIG. 50A

CHO, BHK, 293 cells, Vero expressed Reopro. a-m, r-u (independently selected) = 0 or 1; n = 0; v-y = 0; z = 1.

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3

a-m, r-u (independently selected) = 0 or 1; v-y (independently selected) = 1, when j-m (independently selected) is 1; n = 0; R = PEG; z = 1.

FIG. 50B

Insect cell expressed Reopro. a-h, j-n, s-y = 0; i, r (independently selected) = 0 or 1; z = 1.

1. GNT's 1&2, UDP-GlcNAc-PEG

a-d, f, h, j-n, s, u, w, y = 0;
e, g, i, r, t, v, x (independently selected) = 0 or 1;
v, x (independently selected) = 1,
when e, g (independently selected) is 1;
z = 1; R = PEG.

FIG. 50C

Yeast expressed Reopro.

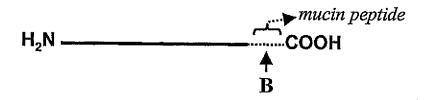
a-n = 0; r-y (independently selected) = 0 to 1;
$$z = 1$$
;

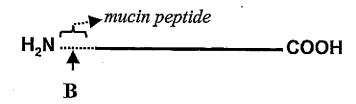
R (branched or linear) = Man, oligomannose or polysaccharide.

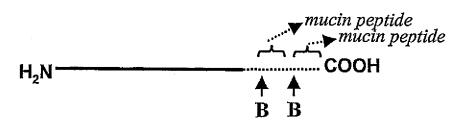
- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal-PEG

a-m, r-z= 0; n = 1; R' = -Gal-PEG.

FIG. 50D







$$\mathbf{B} \leftarrow \begin{bmatrix} (\mathrm{Sia})_{b} \\ -\mathrm{GalNAc} - (\mathrm{Gal})_{a} - (\mathrm{Sia})_{c} - (\mathrm{R})_{d} \end{bmatrix}_{e}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = polymer

FIG. 50E

CHO, BHK, 293 cells, Vero expressed
Reopro-mucin fusion protein.
a-c, e (independently selected) = 0 or 1; d = 0

- 1. Sialidase
 - 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 50F

Insect cell expressed Reopro-mucin fusion protein. a, e (independently selected) = 0 or 1; b, c, d = 0.

1. Galactosyltransferase, UDP-Gal-PEG

a, d, e (independently selected) = 0 or 1; b, c = 0; R = PEG.

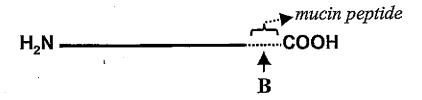
FIG. 50G

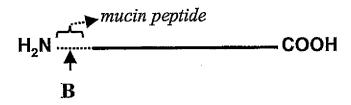
E. coli expressed Reopro-mucin fusion protein. a-e = 0.

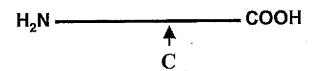
- 1. GalNAc Transferase, UDP-GalNAc
- 2. CMP-SA-PEG, sialyltransferase

```
c, d, e (independently selected) = 0 or 1;
a, b = 0; R = PEG.
```

FIG. 50H







$$\mathbf{B}$$
 \leftarrow $\begin{bmatrix} (\mathrm{Sia})_{b} \\ -\mathrm{GalNAc-(Gal)}_{a} - (\mathrm{Sia})_{c} - (\mathrm{R})_{d} \end{bmatrix}_{e}$

a-c, e (independently selected) = 0 or 1; d = 0; R = polymer, linker.

FIG. 501

E. coli expressed Reopro-mucin fusion protein. a-e, n = 0.

1. GalNAc Transferase, UDP-GalNAc-PEG

d, e (independently selected) = 0 or 1; a-c, n = 0; R = PEG.

FIG. 50J

E. coli expressed Reopro-mucin fusion protein. a-e, n=0.

- GalNAc Transferase,
 UDP-GalNAc-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
- 3. CMP-SA, ST3Gal3

d, e (independently selected) = 0 or 1; a-c, n = 0; R = linker-transferrin.

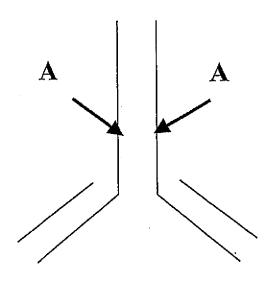
FIG. 50K

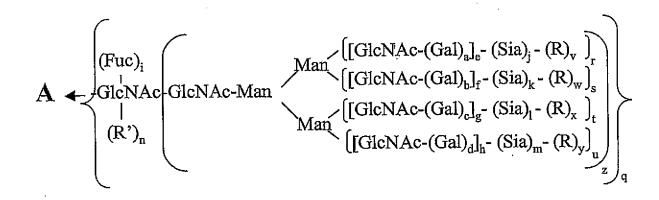
E. coli expressed Reopro(N)—no mucin peptide. a-e, n = 0.

- 1. NHS-CO-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
- 3. CMP-SA, ST3Gal3

a-e=0; n=1; R'=linker-transferrin.

FIG. 50L





a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y = 0; z = 0 or 1; R = polymer, toxin, radioisotopecomplex, drug, glycoconjugate. R' = H, sugar, glycoconjugate.

Z

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed Rituxan.
```

```
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y=0; q, z=1.
```

- 1. galactosyltransferase, UPD-Gal
- 2. CMP-SA-toxin, ST3Gal3

```
a, c, i, j, l (independently selected) = 0 or 1;
e, g, r, t = 1;
f, h, k, m, n, s, u-y = 0; q, z = 1;
v-y (independently selected) = 1,
when j, l (independently selected) is 1;
R = toxin.
```

FIG. 51B

```
CHO, BHK, 293 cells, Vero or fungal expressed Rituxan.
```

```
a, c, e, g, i, r, t (independently selected) = 0 or 1;
b, d, f, h, j-m, n, s, u-y=0; q, z=1.
```

1. galactosyltransferase, UPD-Gal-drug

```
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, j-m, n, s, u-y = 0; q, z = 1;
v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = toxin.
```

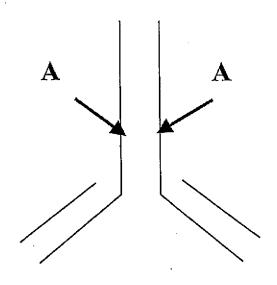
FIG. 51C

Fungi expressed Rituxan. e, g, i, r, t (independently selected) = 0 or 1; a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-radioisotope complex, ST3Gal3

a-m, r-z= 0; q, n = 1; R' = -Gal-Sia-radioisotope complex.

FIG. 51D



$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} \\ \operatorname{GlcNAc-Man} \\ \\ (R')_{n} \end{bmatrix} \begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{a}]_{e} - (\operatorname{Sia})_{j} - (R)_{v} \\ (\operatorname{GlcNAc-(Gal)}_{b}]_{f} - (\operatorname{Sia})_{k} - (R)_{w} \\ \\ (\operatorname{GlcNAc-(Gal)}_{b}]_{g} - (\operatorname{Sia})_{l} - (R)_{x} \\ \\ (\operatorname{GlcNAc-(Gal)}_{d}]_{h} - (\operatorname{Sia})_{m} - (R)_{y} \end{bmatrix}_{u}$$

a-d, i, q-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-m (independently selected) = 0 or 1.
n, v-y = 0; z = 0 or 1;
R = polymer, toxin, radioisotope-complex, drug, glycoconjugate, mannose, oligo-mannose.
R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 51E

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed Rituxan.
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;
q, z = 1.
```

- 1. galactosyltransferase, UPD-Gal
- 2. CMP-SA-PEG, ST3Gal3

```
a, c, i, j, l (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, k, m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when j, l (independently selected) is 1;
R = PEG.
```

FIG. 51F

```
Fungi, yeast or CHO expressed Rituxan.
e, g, i, r, t, v, x (independently selected) = 0 or 1;
a-d, f, h, j-m, n, s, u, w, y = 0; q, z = 1;
R (independently selected) = mannose, oligomannose, polymannose.
```

- 1. mannosidases (alpha and beta)
- 2. GNT-I,II, UDP-GlcNAc
- 3. Galactosyltransferase, UDP-Gal-radioisotope

```
a-m, r-z= 0; q, n = 1;
R' = -Gal-radioisotope complex.
```

FIG. 51G

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FIG. 52A

FIG. 52B

Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gin Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gin Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro

FIG. 53B

Met Ala Leu Thr Phe Ala Leu Leu Val Ala Leu Leu Val Leu Ser Cys Lys Ser Ser Cys Ser Val Gly Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser Leu Arg Ser Lys Glu

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FIG. 54A

ATGACCAACAAGTGTCTCCTCCAAATTGCTCTCCTGTTGTGCTTCTCC ACTACAGCTCTTTCCATGAGCTACAACTTGCTTGGATTCCTACAAAGA AGCAGCAATTTTCAGTGTCAGAAGCTCCTGTGGCAATTGAATGGGAG GCTTGAATATTGCCTCAAGGACAGGATGAACTTTGACATCCCTGAGG AGATTAAGCAGCTGCAGCAGTTCCAGAAGGAGGACGCCGCATTGACC ATCTATGAGATGCTCCAGAACATCTTTGCTATTTTCAGACAAGATTCA TCTAGCACTGGCTGGAATGAGACTATTGTTGAGAACCTCCTGGCTAA TGTCTATCATCAGATAAACCATCTGAAGACAGTCCTGGAAGAAAAAC TGGAGAAAGAAGATTTTACCAGGGGAAAACTCATGAGCAGTCTGCAC CTGAAAAGATATTATGGGAGGATTCTGCATTACCTGAAGGCCAAGGA GTACAGTCACTGTGCCTGGACCATAGTCAGAGTGGAAATCCTAAGGA ACTTTTACTTCATTAACAGACTTACAGGTTACCTCCGAAACTGAAGAT CTCCTAGCCTGTCCCTCTGGGACTGGACAATTGCTTCAAGCATTCTTC AACCAGCAGATGCTGTTTAAGTGACTGATGGCTAATGTACTGCAAAT GAAAGGACACTAGAAGATTTTGAAAATTTTATTAAATTATGAGTTATT TTTATTTAT TTAAATTTTATTTTGGAAAATAAATTATTTTTGGTGC

FIG. 54B

Met Thr Asn Lys Cys Leu Leu Gln Ile Ala Leu Leu Cys Phe Ser Thr Thr Ala Leu Ser Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly ArgLeu Glu Tyr Cys Leu Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn

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FIG. 55A

ATGGTCTCCCAGGCCCTCAGGCTCCTCTGCCTTCTGCTTGGGCTTCAG GGCTGCCTGGCAGTCTTCGTAACCCAGGAGGAAGCCCACGGCGT CCTGCACCGGCGCGCGCCCAACGCGTTCCTGGAGGAGCTGCGGC CGGGCTCCCTGGAGAGGAGTGCAAGGAGGAGCAGTGCTCCTTCGA GGAGGCCCGGAGATCTTCAAGGACGCGGAGAGGACGAAGCTGTTC TGGATTTCTTACAGTGATGGGGACCAGTGTGCCTCAAGTCCATGCCA GAATGGGGGCTCCTGCAAGGACCAGCTCCAGTCCTATATCTGCTTCT GCCTCCCTGCCTTCGAGGGCCGGAACTGTGAGACGCACAAGGATGAC CAGCTGATCTGTGAACGAGAACGGCGGCTGTGAGCAGTACTGCAG TGACCACACGGCCACCAAGCGCTCCTGTCGGTGCCACGAGGGGTACT CTCTGCTGCAGACGGGGTGTCCTGCACACCCACAGTTGAATATCCA TGTGGAAAAATACCTATTCTAGAAAAAAGAAATGCCAGCAAACCCCA AGGCCGAATTGTGGGGGGCAAGGTGTGCCCCAAAGGGGAGTGTCCA TGGCAGGTCCTGTTGTTGGTGAATGGAGCTCAGTTGTGTGGGGGGAC CCTGATCAACACCATCTGGGTGGTCTCCGCGGCCCACTGTTTCGACAA AATCAAGAACTGGAGGAACCTGATCGCGGTGCTGGGCGAGCACGAC CTCAGCGAGCACGACGGGGATGAGCAGAGCCGGCGGGTGGCGCAGG GCGCTGCTCCGCCTGCACCAGCCCGTGGTCCTCACTGACCATGTGGTG CCCCTCTGCCTGCCCGAACGGACGTTCTCTGAGAGGACGCTGGCCTTC GTGCGCTTCTCATTGGTCAGCGGCTGGGGCCAGCTGCTGGACCGTGG CGCCACGCCCTGGAGCTCATGGTGCTCAACGTGCCCCGGCTGATGA CCCAGGACTGCCTGCAGCAGTCACGGAAGGTGGGAGACTCCCCAAAT ATCACGGAGTACATGTTCTGTGCCGGCTACTCGGATGGCAGCAAGGA CTCCTGCAAGGGGACAGTGGAGGCCCACATGCCACCCACTACCGGG GCACGTGGTACCTGACGGGCATCGTCAGCTGGGGCCAGGGCTGCGCA ACCGTGGGCCACTTTGGGGTGTACACCAGGGTCTCCCAGTACATCGA GTGGCTGCAAAAGCTCATGCGCTCAGAGCCACGCCCAGGAGTCCTCC TGCGAGCCCCATTTCCC

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FIG. 55B

Met Val Ser Gln Ala Leu Arg Leu Leu Cys Leu Leu Leu Gly Leu Gln Gly Cys Leu Ala Ala Val Phe Val Thr Gln Glu Glu Ala His Gly Val Leu His Arg Arg Arg Arg Ala Asn Ala Phe Leu Glu Glu Leu Arg Pro Gly Ser Leu Glu Arg Glu Cys Lys Glu Glu Gln Cys Ser Phe Glu Glu Ala Arg Glu Ile Phe Lys Asp Ala Glu Arg Thr Lys Leu Phe Trp Ile Ser Tyr Ser Asp Gly Asp Gln Cys Ala Ser Ser Pro Cys Gln Asn Gly Gly Ser Cys Lys Asp Gln Leu Gln Ser Tyr Ile Cys Phe Cys Leu Pro Ala Phe Glu Gly Arg Asn Cys Glu Thr His Lys Asp Asp Gln Leu Ile Cys Val Asn Glu Asn Gly Gly Cys Glu Gln Tyr Cys Ser Asp His Thr Gly Thr Lys Arg Ser Cys Arg Cys His Glu Gly Tyr Ser Leu Leu Ala Asp Gly Val Ser Cys Thr Pro Thr Val Glu Tyr Pro Cys Gly Lys Ile Pro Ile Leu Glu Lys Arg Asn Ala Ser Lys Pro Gln Gly Arg Ile Val Gly Gly Lys Val Cys Pro Lys Gly Glu Cys Pro Trp Gln Val Leu Leu Val Asn Gly Ala Gln Leu Cys Gly Gly Thr Leu Ile Asn Thr Ile Trp Val Val Ser Ala Ala His Cys Phe Asp Lys Ile Lys Asn Trp Arg Asn Leu Ile Ala Val Leu Gly Glu His Asp Leu Ser Glu His Asp Gly Asp Glu Gln Ser Arg Arg Val Ala Gln Val Ile Ile Pro Ser Thr Tyr Val Pro Gly Thr Thr Asn His Asp Ile Ala Leu Leu Arg Leu His Gln Pro Val Val Leu Thr Asp His Val Val Pro Leu Cys Leu Pro Glu Arg Thr Phe Ser Glu Arg Thr Leu Ala Phe Val Arg Phe Ser Leu Val Ser Gly Trp Gly Gln Leu Leu Asp Arg Gly Ala Thr Ala Leu Glu Leu Met Val Leu Asn Val Pro Arg Leu Met Thr Gln Asp Cys Leu Gln Gln Ser Arg Lys Val Gly Asp Ser Pro Asn Ile Thr Glu Tyr Met Phe Cys Ala Gly Tyr Ser Asp Gly Ser Lys Asp Ser Cys Lys Gly Asp Ser Gly Gly Pro His Ala Thr His Tyr Arg Gly Thr Trp Tyr Leu Thr Gly Ile Val Ser Trp Gly Gln Gly Cys Ala Thr Val Gly His Phe Gly Val Tyr Thr Arg Val Ser Gln Tyr Ile Glu Trp Leu Gln Lys Leu Met Arg Ser Glu Pro Arg Pro Gly Val Leu Leu Arg Ala Pro Phe Pro

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FIG. 56A

ATGCAGCGCGTGAACATGATCATGGCAGAATCACCAAGCCTCATCAC CATCTGCCTTTTAGGATATCTACTCAGTGCTGAATGTACAGTTTTTCTT GATCATGAAAACGCCAACAAAATTCTGAATCGGCCAAAGAGGTATAA GTATGGAAGAAAGTGTAGTTTTGAAGAACCACGAGAAGTTTTTGAA AACACTGAAAAGACAACTGAATTTTGGAAGCAGTATGTTGATGGAGA TCAGTGTGAGTCCAATCCATGTTTAAATGGCGGCAGTTGCAAGGATG ACATTAATTCCTATGAATGTTGGTGTCCCTTTGGATTTGAAGGAAAGA ACTGTGAATTAGATGTAACATGTAACATTAAGAATGGCAGATGCGAG CAGTTTTGTAAAAATAGTGCTGATAACAAGGTGGTTTGCTCCTGTACT GAGGGATATCGACTTGCAGAAAACCAGAAGTCCTGTGAACCAGCAGT GCCATTTCCATGTGGAAGAGTTTCTGTTTCACAAACTTCTAAGCTCAC CCGTGCTGAGGCTGTTTTTCCTGATGTGGACTATGTAAATCCTACTGA AGCTGAAACCATTTTGGATAACATCACTCAAGGCACCCAATCATTTA ATGACTTCACTCGGGTTGTTGGTGGAGAAGATGCCAAACCAGGTCAA TTCCCTTGGCAGGTTGTTTTGAATGGTAAAGTTGATGCATTCTGTGGA GGCTCTATCGTTAATGAAAAATGGATTGTAACTGCTGCCCACTGTGTT GAAACTGGTGTTAAAATTACAGTTGTCGCAGGTGAACATAATATTGA GGAGACAGAACATACAGAGCAAAAGCGAAATGTGATTCGAGCAATT ATTCCTCACCACAACTACAATGCAGCTATTAATAAGTACAACCATGA CATTGCCCTTCTGGAACTGGACGAACCCTTAGTGCTAAACAGCTACG TTACACCTATTTGCATTGCTGACAAGGAATACACGAACATCTTCCTCA AATTTGGATCTGGCTATGTAAGTGGCTGGGCAAGAGTCTTCCACAAA GGGAGATCAGCTTTAGTTCTTCAGTACCTTAGAGTTCCACTTGTTGAC CGAGCCACATGTCTTCGATCTACAAAGTTCACCATCTATAACAACAT GTTCTGTGCTGGCTTCCATGAAGGAGGTAGAGATTCATGTCAAGGAG ATAGTGGGGGACCCCATGTTACTGAAGTGGAAGGGACCAGTTTCTTA ACTGGAATTATTAGCTGGGGTGAAGAGTGTGCAATGAAAGGCAAATA TGGAATATACCAAGGTATCCCGGTATGTCAACTGGATTAAGGAAA AAACAAAGCTCACTTAATGAAAGATGGATTTCCAAGGTTAATTCATT **GGAATTGAAAATTAACAG**

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FIG. 56B

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Ser Leu Ile Thr Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe LeuAsp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys Met Glu Glu Lys Cys Ser Phe Glu Glu Pro Arg Glu Val Phe Glu Asn Thr Glu Lys Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Ala Val Phe Pro Asp Val Asp Tyr Val Asn Pro Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile Thr Gln Gly Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp Gln Val Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg Ala Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asp Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Ala Arg Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Arg Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr

FIG. 57A

FIG. 57B

Met Asp Tyr Tyr Arg Lys Tyr Ala Ala Ile Phe Leu Val Thr Leu Ser Val Phe Leu His Val Leu His Ser Ala Pro Asp Val Gln Asp Cys Pro Glu Cys Thr Leu Gln Glu Asn Pro Phe Phe Ser Gln Pro Gly Ala Pro Ile Leu Gln Cys Met Gly Cys Cys Phe Ser Arg Ala Tyr Pro Thr Pro Leu Arg Ser Lys Lys Thr Met Leu Val Gln Lys Asn Val Thr Ser Glu Ser Thr Cys Cys Val Ala Lys Ser Tyr Asn Arg Val Thr Val Met Gly Gly Phe Lys Val Glu Asn His Thr Ala Cys His Cys Ser Thr Cys Tyr Tyr His Lys Ser

FIG. 57C

FIG. 57D

Met Lys Thr Leu Gln Phe Phe Phe Leu Phe Cys Cys Trp Lys Ala Ile Cys Cys Asn Ser Cys Glu Leu Thr Asn Ile Thr Ile Ala Ile Glu Lys Glu Glu Cys Arg Phe Cys Ile Ser Ile Asn Thr Thr Trp Cys Ala Gly Tyr Cys Tyr Thr Arg Asp Leu Val Tyr Lys Asp Pro Ala Arg Pro Lys Ile Gln Lys Thr Cys Thr Phe Lys Glu Leu Val Tyr Glu Thr Val Arg Val Pro Gly Cys Ala His His Ala Asp Ser Leu Tyr Thr Tyr Pro Val Ala Thr Gln Cys His Cys Gly Lys Cys Asp Ser Asp Ser Thr Asp Cys Thr Val Arg Gly Leu Gly Pro Ser Tyr Cys Ser Phe Gly Glu Met Lys Glu

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FIG. 58A

CCCGGAGCCGGGCCACCGCGCCCGCTCTGCTCCGACACCGC GCCCCTGGACAGCCGCCCTCTCCTCCAGGCCCGTGGGGCTGGCCCT GCACCGCGAGCTTCCCGGGATGAGGGCCCCCGGTGTGGTCACCCGG CGCGCCCAGGTCGCTGAGGGACCCCGGCCAGGCGCGAGATGGGG GTGCACGAATGTCCTGCCTGGCTGTGGCTTCTCCTGTCCCTGCTGTCG CTCCCTCTGGGCCTCCCAGTCCTGGGCGCCCCACCACGCCTCATCTGT GACAGCCGAGTCCTGGAGAGGTACCTCTTGGAGGCCAAGGAGGCCG AGAATATCACGACGGCTGTGCTGAACACTGCAGCTTGAATGAGAAT ATCACTGTCCCAGACACCAAAGTTAATTTCTATGCCTGGAAGAGGAT GGAGGTCGGGCAGCAGGCCGTAGAAGTCTGGCAGGGCCTGGCCCTG CTGTCGGAAGCTGTCCTGCGGGGCCAGGCCCTGTTGGTCAACTCTTCC CAGCCGTGGGAGCCCCTGCAGCTGCATGTGGATAAAGCCGTCAGTGG CCTTCGCAGCCTCACCACTCTGCTTCGGGCTCTGCGAGCCCAGAAGG AAGCCATCTCCCCTCCAGATGCGGCCTCAGCTGCTCCACTCCGAACA ATCACTGCTGACACTTTCCGCAAACTCTTCCGAGTCTACTCCAATTTC CTCCGGGGAAAGCTGAAGCTGTACACAGGGGAGGCCTGCAGGACAG GGGACAGATGACCAGGTGTCCACCTGGGCATATCCACCACCTCCC TCACCAACATTGCTTGTGCCACACCCTCCCCGCCACTCCTGAACCCC GTCGAGGGCTCTCAGCTCAGCGCCAGCCTGTCCCATGGACACTCCA GTGCCAGCAATGACATCTCAGGGGCCAGAGGAACTGTCCAGAGAGC AACTCTGAGATCTAAGGATGTCACAGGGCCAACTTGAGGGCCCAGAG CAGGAAGCATTCAGAGAGCAGCTTTAAACTCAGGGACAGAGCCATG CTGGGAAGACGCCTGAGCTCACTCGGCACCCTGCAAAATTTGATGCC AGGACACGCTTTGGAGGCGATTTACCTGTTTTCGCACCTACCATCAGG GACAGGATGACCTGGAGAACTTAGGTGGCAAGCTGTGACTTCTCCAG GTCTCACGGGCATGGGCACTCCCTTGGTGGCAAGAGCCCCCTTGACA CCGGGGTGGTGGGAACCATGAAGACAGGATGGGGGCTGGCCTCTGG CTCTCATGGGGTCCAAGTTTTGTGTATTCTTCAACCTCATTGACAAGA ACTGAAACCACCAAAAAAAAAAAAAA

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FIG. 58B

Met Gly Val His Glu Cys Pro Ala Trp Leu Trp Leu Leu Leu Ser Leu Leu Ser Leu Pro Leu Gly Leu Pro Val Leu Gly Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Arg Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg Thr Gly Asp Arg

FIG. 59A

ATGTGGCTGCAGAGCCTGCTGCTCTTTGGGCACTGTGGCCTGCAGCAT
CTCTGCACCCGCCCGCTCGCCCAGCCCCAGCACGCAGCCCTGGGAGC
ATGTGAATGCCATCCAGGAGGCCCGGCGTCTCCTGAACCTGAGTAGA
GACACTGCTGCTGAGATGAAACAGTAGAAGTCATCTCAGAAAT
GTTTGACCTCCAGGAGCCGACCTGCCTACAGACCCGCCTGGAGCTGT
ACAAGCAGGGCCTGCGGGGCAGCCTCACCAAGCTCAAGGGCCCCTTG
ACCATGATGGCCAGCCACTACAAGCAGCACTGCCCTCCAACCCCGGA
AACTTCCTGTGCAACCCAGATTATCACCTTTGAAAGTTTCAAAGAGA
ACCTGAAGGACTTTCTGCTTGTCATCCCCTTTGACTGCTGGGAGCCAG
TCCAGGAGTGA

FIG. 59B

Met Trp Leu Gln Ser Leu Leu Leu Leu Gly Thr Val Ala Cys Ser Ile Ser Ala Pro Ala Arg Ser Pro Ser Pro Ser Thr Gln Pro Trp Glu His Val Asn Ala Ile Gln Glu Ala Arg Arg Leu Leu Asn Leu Ser Arg Asp Thr Ala Ala Glu Met Asn Glu Thr Val Glu Val Ile Ser Glu Met Phe Asp Leu Gln Glu Pro Thr Cys Leu Gln Thr Arg Leu Glu Leu Tyr Lys Gln Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro Leu Thr Met Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr Pro Glu Thr Ser Cys Ala Thr Gln Ile Ile Thr Phe Glu Ser Phe Lys Glu Asn Leu Lys Asp Phe Leu Leu Val Ile Pro Phe Asp Cys Trp Glu Pro Val Gln Glu

FIG. 60A

ATGAAATATACAAGTTATATCTTGGCTTTTCAGCTCTGCATCGTTTTG
GGTTCTCTTGGCTGTTACTGCCAGGACCCATATGTAAAAAGAAGCAGA
AAACCTTAAGAAATATTTTAATGCAGGTCATTCAGATGTAGCGGATA
ATGGAACTCTTTTCTTAGGCATTTTGAAGAATTGGAAAAGAGGAGAGT
GACAGAAAAATAATGCAGAGCCAAATTGTCTCCTTTTACTTCAAACT
TTTTAAAAAACTTTAAAGATGACCAGAGCATCCAAAAGAGTGTGGAGA
CCATCAAGGAAGACATGAATGTCAAGTTTTTCAATAGCAACAAAAAG
AAACGAGATGACTTCGAAAAAGCTGACTAATTATTCGGTAACTGACTT
GAATGTCCAACGCAAAGCAATACATGAACTCATCCAAGTGATGGCTG
AACTGTCGCCAGCAGCTAAAAACAGGGAAAAAAGGAGTCAGAT
GCTGTTTCGAGGTCGAAGAGCATCCCAGTAA

FIG. 60B

Met Lys Tyr Thr Ser Tyr Ile Leu Ala Phe Gln Leu Cys Ile Val Leu Gly Ser Leu Gly Cys Tyr Cys Gln Asp Pro Tyr Val Lys Glu Ala Glu Asn Leu Lys Lys Tyr Phe Asn Ala Gly His Ser Asp Val Ala Asp Asn Gly Thr Leu Phe Leu Gly Ile Leu Lys Asn Trp Lys Glu Glu Ser Asp Arg Lys Ile Met Gln Ser Gln Ile Val Ser Phe Tyr Phe Lys Leu Phe Lys Asn Phe Lys Asp Asp Gln Ser Ile Gln Lys Ser Val Glu Thr Ile Lys Glu Asp Met Asn Val Lys Phe Phe Asn Ser Asn Lys Lys Arg Asp Asp Phe Glu Lys Leu Thr Asn Tyr Ser Val Thr Asp Leu Asn Val Gln Arg Lys Ala Ile His Glu Leu Ile Gln Val Met Ala Glu Leu Ser Pro Ala Ala Lys Thr Gly Lys Arg Lys Arg Ser Gln Met Leu Phe Arg Gly Arg Arg Ala Ser Gln

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FIG. 61A

CTGGGACAGTGAATCGACAATGCCGTCTTCTGTCTCGTGGGGCATCCT CCTGCTGGCAGGCCTGTGCTGCCTGGTCCCTGTCTCCCTGGCTGAGGA TCCCCAGGGAGATGCTGCCCAGAAGACAGATACATCCCACCATGATC AGGATCACCCAACCTTCAACAAGATCACCCCCAACCTGGCTGAGTTC GCCTTCAGCCTATACCGCCAGCTGGCACACCAGTCCAACAGCACCAA TATCTTCTCCCCAGTGAGCATCGCTACAGCCTTTGCAATGCTCTC CCTGGGGACCAAGGCTGACACTCACGATGAAATCCTGGAGGCCTGA ATTTCAACCTCACGGAGATTCCGGAGGCTCAGATCCATGAAGGCTTC GACCACCGGCAATGGCCTGTTCCTCAGCGAGGGCCTGAAGCTAGTGG ATAAGTTTTTGGAGGATGTTAAAAAGTTGTACCACTCAGAAGCCTTC ACTGTCAACTTCGGGGACACCGAAGAGGCCAAGAAACAGATCAACG ATTACGTGGAGAAGGGTACTCAAGGGAAAATTGTGGATTTGGTCAAG GAGCTTGACAGAGACACAGTTTTTGCTCTGGTGAATTACATCTTCTTT AAAGGCAAATGGGAGAGACCCTTTGAAGTCAAGGACACCGAGGAAG AGGACTTCCACGTGGACCAGGTGACCACCGTGAAGGTGCCTATGATG AAGCGTTTAGGCATGTTAACATCCAGCACTGTAAGAAGCTGTCCAG CTGGGTGCTGCTGATGAAATACCTGGGCAATGCCACCGCCATCTTCT TCCTGCCTGATGAGGGGAAACTACAGCACCTGGAAAATGAACTCACC CACGATATCATCACCAAGTTCCTGGAAAATGAAGACAGAAGGTCTGC CAGCTTACATTTACCCAAACTGTCCATTACTGGAACCTATGATCTGAA GAGCGTCCTGGGTCAACTGGGCATCACTAAGGTCTTCAGCAATGGGG CTGACCTCTCCGGGGTCACAGAGGAGGCACCCCTGAAGCTCTCCAAG GCCGTGCATAAGGCTGTGCTGACCATCGACGAGAAAGGGACTGAAGC TGCTGGGGCCATGTTTTTAGAGGCCATACCCATGTCTATCCCCCCGA GGTCAAGTTCAACAAACCCTTTGTCTTCTTAATGATTGAACAAAATAC AACTGCCTCTCGCTCCTCAACCCCTCCCTCCATCCCTGGCCCCCTCC CTGGATGACATTAAAGAAGGGTTGAGCTGG

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FIG. 61B

Met Pro Ser Ser Val Ser Trp Gly Ile Leu Leu Leu Ala Gly Leu Cys Cys Leu Val Pro Val Ser Leu Ala Glu Asp Pro Gln Gly Asp Ala Ala Gln Lys Thr Asp Thr Ser His His Asp Gln Asp His Pro Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu Phe Ala Phe Ser Leu Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr Asn Ile Phe Phe Ser Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu Ser Leu Gly Thr Lys Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu Asn Phe Asn Leu Thr Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe Gln Glu Leu Leu Arg Thr Leu Asn Gln Pro Asp Ser Gln Leu Gln Leu Thr Thr Gly Asn Gly Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp Lys Phe Leu Glu Asp Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr Val Asn Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr Val Glu Lys Gly Thr Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu Asp Arg Asp Thr Val Phe Ala LeuVal Asn Tyr Ile Phe Phe Lys Gly Lys Trp Glu Arg Pro Phe Glu Val Lys Asp Thr Glu Glu Glu Asp Phe His Val Asp Gln Val Thr Thr Val Lys Val Pro Met Met Lys Arg Leu Gly Met Phe Asn Ile Gln His Cys Lys Lys Leu Ser Ser Trp Val Leu Leu Met Lys Tyr Leu Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp Glu Gly Lys Leu Gln His Leu Glu Asn Glu Leu Thr His Asp Ile Ile Thr Lys Phe Leu Glu Asn Glu AspArg Arg Ser Ala Ser Leu His Leu Pro Lys Leu Ser Ile Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly Gln Leu Gly Ile Thr Lys Val Phe Ser Asn Gly Ala Asp Leu Ser Gly Val Thr Glu Glu Ala Pro Leu Lys Leu Ser Lys Ala Val His Lys Ala Val Leu Thr Ile Asp Glu Lys Gly Thr Glu Ala Ala Gly Ala Met Phe Leu Glu Ala Ile Pro Met Ser Ile Pro Pro Glu Val Lys Phe Asn Lys Pro Phe Val Phe Leu Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe Met Gly Lys Val Val Asn Pro Thr Gln Lys

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GCTAACCTAGTGCCTATAGCTAAGGCAGGTACCTGCATCCTTGTTTTT GTTTAGTGGATCCTCTATCCTTCAGAGACTCTGGAACCCCTGTGGTCT TCTCTTCATCTAATGACCCTGAGGGGATGGAGTTTTCAAGTCCTTCCA AGCCTCACAGGTTTGCTTCTACTTCAGGCAGTGTCGTGGGCATCAGGT GCCCGCCCTGCATCCCTAAAAGCTTCGGCTACAGCTCGGTGGTGTGT GTCTGCAATGCCACATACTGTGACTCCTTTGACCCCCGACCTTTCCT GCCCTTGGTACCTTCAGCCGCTATGAGAGTACACGCAGTGGGCGACG GATGGAGCTGAGTATGGGGCCCATCCAGGCTAATCACACGGGCACAG GCCTGCTACTGACCCTGCAGCCAGAACAGAAGTTCCAGAAAGTGAAG GGATTTGGAGGGCCATGACAGATGCTGCTCTCAACATCCTTGCC CTGTCACCCCCTGCCCAAAATTTGCTACTTAAATCGTACTTCTCTGAA GAAGGAATCGGATATAACATCATCCGGGTACCCATGGCCAGCTGTGA CTTCTCCATCCGCACCTACACCTATGCAGACACCCCTGATGATTTCCA GTTGCACAACTTCAGCCTCCCAGAGGAAGATACCAAGCTCAAGATAC CCCTGATTCACCGAGCCCTGCAGTTGGCCCAGCGTCCCGTTTCACTCC TTGCCAGCCCTGGACATCACCCACTTGGCTCAAGACCAATGGAGCG GTGAATGGGAAGGGTCACTCAAGGGACAGCCCGGAGACATCTACC ACCAGACCTGGGCCAGATACTTTGTGAAGTTCCTGGATGCCTATGCTG AGCACAAGTTACAGTTCTGGGCAGTGACAGCTGAAAATGAGCCTTCT GCTGGGCTGTTGAGTGGATACCCCTTCCAGTGCCTGGGCTTCACCCCT GAACATCAGCGAGACTTCATTGCCCGTGACCTAGGTCCTACCCTCGCC AACAGTACTCACCACAATGTCCGCCTACTCATGCTGGATGACCAACGC TTGCTGCTGCCCCACTGGGCAAAGGTGGTACTGACAGACCCAGAAGC AGCTAAATATGTTCATGGCATTGCTGTACATTGGTACCTGGACTTTCT GGCTCCAGCCAAAGCCACCCTAGGGGAGACACACCGCCTGTTCCCCA ACACCATGCTCTTTGCCTCAGAGGCCTGTGTGGGCTCCAAGTTCTGGG AGCAGAGTGTGCGGCTAGGCTCCTGGGATCGAGGGATGCAGTACAGC CACAGCATCATCACGAACCTCCTGTACCATGTGGTCGGCTGGACCGAC TGGAACCTTGCCCTGAACCCCGAAGGAGGACCCAATTGGGTGCGTAA CTTTGTCGACAGTCCCATCATTGTAGACATCACCAAGGACACGTTTTA CAAACAGCCCATGTTCTACCACCTTGGCCACTTCAGCAAGTTCATTCC TGAGGGCTCCCAGAGAGTGGGGCTGGTTGCCAGTCAGAAGAACGACC TGGACGCAGTGGCACTGATGCATCCCGATGGCTCTGCTGTTGTGGTCG TGCTAAACCGCTCCTCTAAGGATGTGCCTCTTACCATCAAGGATCCTG CTGTGGGCTTCCTGGAGACAATCTCACCTGGCTACTCCATTCACACCT ACCTGTGGCATCGCCAGTGATGGAGCAGATACTCAAGGAGGCACTGG GCTCAGCCTGGGCATTAAAGGGACAGAGTCAGCTCACACGCTGTCTG TGACTAAAGAGGCACAGCAGGGCCAGTGTGAGCTTACAGCGACGT

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FIG. 62A-2

FIG. 62B

Met Glu Phe Ser Ser Pro Ser Arg Glu Glu Cys Pro Lys Pro Leu Ser Arg Val Ser Ile Met Ala Gly Ser Leu Thr Gly Leu Leu Leu Leu Gln Ala Val Ser Trp Ala Ser Gly Ala Arg Pro Cys Ile Pro Lys Ser Phe Gly Tyr Ser Ser Val Val Cys Val Cys Asn Ala Thr Tyr Cys Asp Ser Phe Asp Pro Pro Thr Phe Pro Ala Leu Gly Thr Phe Ser Arg Tyr Glu Ser Thr Arg Ser Gly Arg Arg Met Glu Leu Ser Met Gly Pro Ile Gln Ala Asn His Thr Gly Thr Gly Leu Leu Leu Thr Leu Gln Pro Glu Gln Lys Phe Gln Lys Val Lys Gly Phe Gly Gly Ala Met Thr Asp Ala Ala Ala Leu Asn Ile Leu Ala Leu Ser Pro Pro Ala Gln Asn Leu Leu Leu Lys Ser Tyr Phe Ser Glu Glu Gly Ile Gly Tyr Asn Ile Ile Arg Val Pro Met Ala Ser Cys Asp Phe Ser Ile Arg Thr Tyr Thr Tyr Ala Asp Thr Pro Asp Asp Phe Gln Leu His Asn Phe Ser Leu Pro Glu Glu Asp Thr Lys Leu Lys Ile Pro Leu Ile His Arg Ala Leu Gln Leu Ala Gln Arg Pro Val Ser Leu Leu Ala Ser Pro Trp Thr Ser Pro Thr Trp Leu Lys Thr Asn Gly Ala Val Asn Gly Lys Gly Ser Leu Lys Gly Gln Pro Gly Asp Ile Tyr His Gln Thr Trp Ala Arg Tyr Phe Val Lys Phe Leu Asp Ala Tyr Ala Glu His Lys Leu Gln Phe Trp Ala Val Thr Ala Glu Asn Glu Pro Ser Ala Gly Leu Leu Ser Gly Tyr Pro Phe Gln Cys Leu Gly Phe Thr Pro Glu His Gln Arg Asp Phe Ile Ala Arg Asp Leu Gly Pro Thr Leu Ala Asn Ser Thr His His Asn Val Arg Leu Leu Met Leu Asp Asp Gln Arg Leu Leu Leu Pro His Trp Ala Lys Val Val Leu Thr Asp Pro Glu Ala Ala Lys Tyr Val His Gly Ile Ala Val His Trp Tyr Leu Asp Phe Leu Ala Pro Ala Lys Ala Thr Leu Gly Glu Thr His Arg Leu Phe Pro Asn Thr Met Leu Phe Ala Ser Glu Ala Cys Val Gly Ser Lys Phe Trp Glu Gln Ser Val Arg Leu Gly Ser Trp Asp Arg Gly Met Gln Tyr Ser His Ser Ile Ile Thr Asn Leu Leu Tyr His Val Val Gly Trp Thr Asp Trp Asn Leu Ala Leu Asn Pro Glu Gly Gly Pro Asn Trp Val Arg Asn Phe Val Asp Ser Pro Ile Ile Val Asp Ile Thr Lys Asp Thr Phe Tyr Lys Gln Pro Met Phe Tyr His Leu Gly His Phe Ser Lys Phe Ile Pro Glu Gly Ser Gln Arg Val Gly Leu Val Ala Ser Gln Lys Asn Asp Leu Asp Ala Val Ala Leu Met His Pro Asp Gly Ser Ala Val Val Val Leu Asn Arg Ser Ser Lys Asp Val Pro Leu Thr Ile Lys Asp Pro Ala Val Gly Phe Leu Glu Thr Ile Ser Pro Gly Tyr Ser Ile His Thr Tyr Leu Trp His Arg Gln

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ATGGATGCAATGAAGAGAGGGCTCTGCTGTGTGTGCTGCTGTGTGG AGCAGTCTTCGTTTCGCCCAGCCAGGAAATCCATGCCCGATTCAGAA GAGGAGCCAGATCTTACCAAGTGATCTGCAGAGATGAAAAAACGCA GATGATATACCAGCAACATCAGTCATGGCTGCGCCCTGTGCTCAGAA GCAACCGGGTGGAATATTGCTGGTGCAACAGTGGCAGGGCACAGTGC CACTCAGTGCCTGTCAAAAGTTGCAGCGAGCCAAGGTGTTTCAACGG GGGCACCTGCCAGCAGGCCCTGTACTTCTCAGATTTCGTGTGCCAGTG CCCCGAAGGATTTGCTGGGAAGTGCTGTGAAATAGATACCAGGGCCA CGTGCTACGAGGACCAGGGCATCAGCTACAGGGGCACGTGGAGCAC AGCGGAGAGTGGCGCCGAGTGCACCAACTGGAACAGCAGCGCGTTG GCCCAGAAGCCCTACAGCGGGCGGAGGCCAGACGCCATCAGGCTGG GCCTGGGGAACCACAACTACTGCAGAAACCCAGATCGAGACTCAAA GCCCTGGTGCTACGTCTTTAAGGCGGGGAAGTACAGCTCAGAGTTCT GCAGCACCCCTGCCTGCTCTGAGGGAAACAGTGACTGCTACTTTGGG AATGGGTCAGCCTACCGTGGCACGCACAGCCTCACCGAGTCGGGTGC CTCCTGCCTCCCGTGGAATTCCATGATCCTGATAGGCAAGGTTTACAC AGCACAGAACCCCAGTGCCCAGGCACTGGGCCTGGGCAAACATAATT ACTGCCGGAATCCTGATGGGGATGCCAAGCCCTGGTGCCACGTGCTG AAGAACCGCAGGCTGACGTGGGAGTACTGTGATGTGCCCTCCTGCTC CACCTGCGGCCTGAGACAGTACAGCCAGCCTCAGTTTCGCATCAAAG GAGGGCTCTTCGCCGACATCGCCTCCCACCCCTGGCAGGCTGCCATCT TTGCCAAGCACAGGAGGTCGCCGGGAGAGCGGTTCCTGTGCGGGGGC ATACTCATCAGCTCCTGCTGGATTCTCTCTGCCGCCCACTGCTTCCAG GAGAGGTTTCCGCCCCACCACCTGACGGTGATCTTGGGCAGAACATA CCGGGTGGTCCCTGGCGAGGAGGAGCAGAAATTTGAAGTCGAAAAA TACATTGTCCATAAGGAATTCGATGATGACACTTACGACAATGACAT TGCGCTGCAGCTGAAATCGGATTCGTCCCGCTGTGCCCAGGAGA GCAGCGTGGTCCGCACTGTGTGCCTTCCCCCGGCGGACCTGCAGCTG CCGGACTGGACGGAGTGTGAGCTCTCCGGCTACGGCAAGCATGAGGC CTTGTCTCCTTTCTATTCGGAGCGCTGAAGGAGGCTCATGTCAGACT GTACCCATCCAGCCGCTGCACATCACAACATTTACTTAACAGAACAG TCACCGACAACATGCTGTGTGCTGGAGACACTCGGAGCGGCGGCCC CAGGCAAACTTGCACGACGCCTGCCAGGGCGATTCGGGAGGCCCCCT GGTGTGTCTGAACGATGGCCGCATGACTTTGGTGGGCATCATCAGCT GGGCCTGGGCTGTGGACAGAAGGATGTCCCGGGTGTGTACACCAAG GTTACCAACTACCTAGACTGGATTCGTGACAACATGCGACCGTGACC AGGAACACCCGACTCCTCAAAAGCAAATGAGATCC

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FIG. 63B

Met Asp Ala Met Lys Arg Gly Leu Cys Cys Val Leu Leu Cys Gly Ala Val Phe Val Ser Pro Ser Gln Glu Ile His Ala Arg Phe Arg Arg Gly Ala Arg Ser Tyr Gln Val Ile Cys Arg Asp Glu Lys Thr Gln Met Ile Tyr Gln Gln His Gln Ser Trp Leu Arg Pro Val Leu Arg Ser Asn Arg Val Glu Tyr Cys Trp Cys Asn Ser Gly Arg Ala Gln Cys His Ser Val Pro Val Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn Gly Gly Thr Cys Gln Gln Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro Glu Gly Phe Ala Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr Glu Asp Gln Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala Glu Ser Gly Ala Glu Cys Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro Tyr Ser Gly Arg Arg Pro Asp Ala Ile Arg Leu Gly Leu Gly Asn His Asn Tyr Cys Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys Tyr Val Phe Lys Ala Gly Lys Tyr Ser Ser Glu Phe Cys Ser Thr Pro Ala Cys Ser Glu Gly Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg Gly Thr His Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn Ser Met Ile Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro Gln Phe Arg Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Glu Lys Phe Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys Glu Ala His Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met

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ATCACTCTCTTTAATCACTACTCACATTAACCTCAACTCCTGCCACAA TGTACAGGATGCAACTCCTGTCTTGCATTGCACTAATTCTTGCACTTG TCACAAACAGTGCACCTACTTCAAGTTCGACAAAGAAAACAAAGAAA ACACAGCTACAACTGGAGCATTTACTGCTGGATTTACAGATGATTTTG AATGGAATTAATAATTACAAGAATCCCAAACTCACCAGGATGCTCAC ATTTAAGTTTTACATGCCCAAGAAGGCCACAGAACTGAAACAGCTTC AGTGTCTAGAAGAAGAACTCAAACCTCTGGAGGAAGTGCTGAATTTA GCTCAAAGCAAAACTTTCACTTAAGACCCAGGGACTTAATCAGCAA TATCAACGTAATAGTTCTGGAACTAAAGGGATCTGAAACAACATTCA TGTGTGAATATGCAGATGAGACAGCAACCATTGTAGAATTTCTGAAC AGATGGATTACCTTTTGTCAAAGCATCATCTCAACACTAACTTGATAA AATATTTAAATTTTATATTTGTTGAATGTATGGTTGCTACCTATTG TAACTATTATTCTTAATCTTAAAACTATAAAATATGGATCTTTTATGAT CAAAAATATTATTATTATGTTGAATGTTAAATATAGTATCTATGTAG AAACAAAAAAAAAAA

FIG. 64B

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ile Leu Ala Leu Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Lys Lys Thr Gln Leu Gln Leu Glu His Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys Gln Leu Gln Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr

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ATGCAAATAGAGCTCTCCACCTGCTTCTTTCTGTGCCTTTTTGCGATTCT GCTTTAGTGCCACCAGAAGATACTACCTGGGTGCAGTGGAACTGTCA TGGGACTATATGCAAAGTGATCTCGGTGAGCTGCCTGTGGACGCAAG ATTTCCTCCTAGAGTGCCAAAATCTTTTCCATTCAACACCTCAGTCGT GTACAAAAAGACTCTGTTTGTAGAATTCACGGATCACCTTTTCAACAT CGCTAAGCCAAGGCCACCCTGGATGGGTCTGCTAGGTCCTACCATCC AGGCTGAGGTTTATGATACAGTGGTCATTACACTTAAGAACATGGCT TCCCATCCTGTCAGTCTTCATGCTGTTGGTGTATCCTACTGGAAAGCT TCTGAGGGAGCTGAATATGATGATCAGACCAGTCAAAGGGAGAAAG AAGATGATAAAGTCTTCCCTGGTGGAAGCCATACATATGTCTGGCAG GTCCTGAAAGAGAATGGTCCAATGGCCTCTGACCCACTGTGCCTTAC CTACTCATATCTTCTCATGTGGACCTGGTAAAAGACTTGAATTCAGG CCTCATTGGAGCCCTACTAGTATGTAGAGAAGGGAGTCTGGCCAAGG AAAAGACACAGACCTTGCACAAATTTATACTACTTTTTGCTGTATTTG ATGAAGGGAAAAGTTGGCACTCAGAAACAAAGAACTCCTTGATGCA GGATAGGGATGCTGCATCTGCTCGGGCCTGGCCTAAAATGCACACAG TCAATGGTTATGTAAACAGGTCTCTGCCAGGTCTGATTGGATGCCACA GGAAATCAGTCTATTGGCATGTGATTGGAATGGGCACCACTCCTGAA GTGCACTCAATATTCCTCGAAGGTCACACATTTCTTGTGAGGAACCAT CGCCAGGCGTCCTTGGAAATCTCGCCAATAACTTTCCTTACTGCTCAA ACACTCTTGATGGACCTTGGACAGTTTCTACTGTTTTGTCATATCTCTT CCCACCAACATGATGGCATGGAAGCTTATGTCAAAGTAGACAGCTGT CCAGAGGAACCCCAACTACGAATGAAAAATAATGAAGAAGCGGAAG ACTATGATGATGATCTTACTGATTCTGAAATGGATGTGGTCAGGTTTG ATGATGACAACTCTCCTTCCTTTATCCAAATTCGCTCAGTTGCCAAGA AGCATCCTAAAACTTGGGTACATTACATTGCTGCTGAAGAGGAGGAC TGGGACTATGCTCCCTTAGTCCTCGCCCCCGATGACAGAAGTTATAAA AGTCAATATTTGAACAATGGCCCTCAGCGGATTGGTAGGAAGTACAA AAAAGTCCGATTTATGGCATACACAGATGAAACCTTTAAGACTCGTG AAGCTATTCAGCATGAATCAGGAATCTTGGGACCTTTACTTTATGGGG TCAAGGAGATTACCAAAAGGTGTAAAAACATTTGAAGGATTTTCCAAT TCTGCCAGGAGAAATATTCAAATATAAATGGACAGTGACTGTAGAAG ATGGGCCAACTAAATCAGATCCTCGGTGCCTGACCCGCTATTACTCTA GTTTCGTTAATATGGAGAGAGATCTAGCTTCAGGACTCATTGGCCCTC TCCTCATCTGCTACAAAGAATCTGTAGATCAAAGAGGAAACCAGATA ATGTCAGACAAGAGGAATGTCATCCTGTTTTCTGTATTTGATGAGAAC CGAAGCTGGTACCTCACAGAGAATATACAACGCTTTCTCCCCAATCCA GCTGGAGTGCAGCTTGAGGATCCAGAGTTCCAAGCCTCCAACATCAT GCACAGCATCAATGGCTATGTTTTTGATAGTTTGCAGTTGTCAGTTTG TTTGCATGAGGTGGCATACTGGTACATTCTAAGCATTGGAGCACAGA CTGACTTCCTTTCTCTCTCTCTGGATATACCTTCAAACACAAAAAT

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GGTCTATGAAGACACACTCACCCTATTCCCATTCTCAGGAGAAACTGT CTTCATGTCGATGGAAAACCCAGGTCTATGGATTCTGGGGTGCCACA ACTCAGACTTTCGGAACAGAGGCATGACCGCCTTACTGAAGGTTTCT AGTTGTGACAAGAACACTGGTGATTATTACGAGGACAGTTATGAAGA TATTTCAGCATACTTGCTGAGTAAAAACAATGCCATTGAACCAAGAA GCTTCTCCCAGAATTCAAGACACCGTAGCACTAGGCAAAAGCAATTT AATGCCACCACAATTCCAGAAAATGACATAGAGAAGACTGACCCTTG GTTTGCACACAGAACACCTATGCCTAAAATACAAAATGTCTCCTCTA GTGATTTGTTGATGCTCTTGCGACAGAGTCCTACTCCACATGGGCTAT CCTTATCTGATCTCCAAGAAGCCAAATATGAGACTTTTTCTGATGATC CATCACCTGGAGCAATAGACAGTAATAACAGCCTGTCTGAAATGACA CACTTCAGGCCACAGCTCCATCACAGTGGGGACATGGTATTTACCCC TGAGTCAGGCCTCCAATTAAGATTAAATGAGAAACTGGGGACAACTG CAGCAACAGAGTTGAAGAAACTTGATTTCAAAGTTTCTAGTACATCA AATAATCTGATTTCAACAATTCCATCAGACAATTTGGCAGCAGGTACT GATAATACAAGTTCCTTAGGACCCCCAAGTATGCCAGTTCATTATGAT AGTCAATTAGATACCACTCTATTTGGCAAAAAGTCATCTCCCCTTACT GAGTCTGGTGGACCTCTGAGCTTGAGTGAAGAAAATAATGATTCAAA GTTGTTAGAATCAGGTTTAATGAATAGCCAAGAAAGTTCATGGGGAA AAAATGTATCGTCAACAGAGAGTGGTAGGTTATTTAAAGGGAAAAGA GCTCATGGACCTGCTTTGTTGACTAAAGATAATGCCTTATTCAAAGTT AGCATCTCTTTGTTAAAGACAAACAAAACTTCCAATAATTCAGCAACT AATAGAAAGACTCACATTGATGGCCCATCATTATTAATTGAGAATAG TCCATCAGTCTGGCAAAATATATTAGAAAGTGACACTGAGTTTAAAA AAGTGACACCTTTGATTCATGACAGAATGCTTATGGACAAAAATGCT ACAGCTTTGAGGCTAAATCATATGTCAAATAAAACTACTTCATCAAA AAACATGGAAATGGTCCAACAGAAAAAAGAGGGCCCCATTCCACCA GATGCACAAAATCCAGATATGTCGTTCTTTAAGATGCTATTCTTGCCA GAATCAGCAAGGTGGATACAAAGGACTCATGGAAAGAACTCTCTGAA CTCTGGGCAAGGCCCCAGTCCAAAGCAATTAGTATCCTTAGGACCAG AAAAATCTGTGGAAGGTCAGAATTTCTTGTCTGAGAAAAAACAAAGTG GTAGTAGGAAAGGGTGAATTTACAAAGGACGTAGGACTCAAAGAGA TGGTTTTTCCAAGCAGCAGAAACCTATTTCTTACTAACTTGGATAATT TACATGAAAATAATACACACAATCAAGAAAAAAAAAATTCAGGAAGA AATAGAAAAGAAGGAAACATTAATCCAAGAGAATGTAGTTTTGCCTC AGATACATACAGTGACTGGCACTAAGAATTTCATGAAGAACCTTTTC TTACTGAGCACTAGGCAAAATGTAGAAGGTTCATATGACGGGGCATA TGCTCCAGTACTTCAAGATTTTAGGTCATTAAATGATTCAACAAATAG AACAAAGAAACACACAGCTCATTTCTCAAAAAAAGGGGAGGAAGAA AACTTGGAAGGCTTGGGAAATCAAACCAGCAAATTGTAGAGAAATAT GCATGCACCACAAGGAATATCTCCTAATACAAGCCAGCAGAATTTTG TCACGCAACGTAGTAAGAGAGCTTTGAAACAATTCAGACTCCCACTA

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GAAGAAACAGAACTTGAAAAAAGGATAATTGTGGATGACACCTCAAC CCAGTGGTCCAAAAACATGAAACATTTGACCCCGAGCACCCTCACAC AGATAGACTACAATGAGAAGGAGAAAGGGGCCATTACTCAGTCTCCC TTATCAGATTGCCTTACGAGGAGTCATAGCATCCCTCAAGCAAATAGA TCTCCATTACCCATTGCAAAGGTATCATCATTTCCATCTATTAGACCTA TATATCTGACCAGGGTCCTATTCCAAGACAACTCTTCTCATCTTCCAG CAGCATCTTATAGAAAGAAAGATTCTGGGGTCCAAGAAAGCAGTCAT TTCTTACAAGGAGCCAAAAAAAAAATAACCTTTCTTTAGCCATTCTAACC TTGGAGATGACTGGTGATCAAAGAGAGGTTGGCTCCCTGGGGACAAG TGCCACAAATTCAGTCACATACAAGAAAGTTGAGAACACTGTTCTCCC GAAACCAGACTTGCCCAAAACATCTGGCAAAGTTGAATTGCTTCCAA AAGTTCACATTTATCAGAAGGACCTATTCCCTACGGAAACTAGCAATG GGTCTCCTGGCCATCTGGATCTCGTGGAAGGGAGCCTTCTTCAGGGAA CAGAGGGAGCGATTAAGTGGAATGAAGCAAACAGACCTGGAAAAGT GCTATTGGATCCTCTTGCTTGGGATAACCACTATGGTACTCAGATACC AAAAGAAGAGTGGAAATCCCAAGAGAAGTCACCAGAAAAAACAGCT TTTAAGAAAAAGGATACCATTTTGTCCCTGAACGCTTGTGAAAGCAAT CATGCAATAGCAGCAATAAATGAGGGACAAAATAAGCCCGAAATAG AAGTCACCTGGGCAAAGCAAGGTAGGACTGAAAGGCTGTGCTCTCAA AACCCACCAGTCTTGAAACGCCATCAACGGGAAATAACTCGTACTAC TCTTCAGTCAGATCAAGAGGAAATTGACTATGATGATACCATATCAGT TGAAATGAAGAAGGAAGATTTTGACATTTATGATGAGGATGAAAATC CAGTGGAGAGGCTCTGGGATTATGGGATGAGTAGCTCCCCACATGTT CTAAGAAACAGGGCTCAGAGTGGCAGTGTCCCTCAGTTCAAGAAAGT TGTTTTCCAGGAATTTACTGATGGCTCCTTTACTCAGCCCTTATACCGT GGAGAACTAAATGAACATTTGGGACTCCTGGGGCCATATATAAGAGC AGAAGTTGAAGATAATATCATGGTAACTTTCAGAAATCAGGCCTCTC GTCCCTATTCCTATTCTAGCCTTATTTCTTATGAGGAAGATCAGAG GCAAGGAGCAGAACCTAGAAAAAACTTTGTCAAGCCTAATGAAACCA AAACTTACTTTTGGAAAGTGCAACATCATATGGCACCCACTAAAGAT GAGTTTGACTGCAAAGCCTGGGCTTATTTCTCTGATGTTGACCTGGAA AAAGATGTGCACTCAGGCCTGATTGGACCCCTTCTGGTCTGCCACACT AACACACTGAACCCTGCTCATGGGAGACAAGTGACAGTACAGGAATT TGCTCTGTTTTCACCATCTTTGATGAGACCAAAAGCTGGTACTTCACT GAAAATATGGAAAGAAACTGCAGGGCTCCCTGCAATATCCAGATGGA CATAATGGATACACTACCTGGCTTAGTAATGGCTCAGGATCAAAGGA TTCGATGGTATCTGCTCAGCATGGGCAGCAATGAAAACATCCATTCT TAAAATGGCACTGTACAATCTCTATCCAGGTGTTTTTTGAGACAGTGGA

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AATGTTACCATCCAAAGCTGGAATTTGGCGGGTGGAATGCCTTATTGG CGAGCATCTACATGCTGGGATGAGCACACTTTTTCTGGTGTACAGCAA TAAGTGTCAGACTCCCCTGGGAATGGCTTCTGGACACATTAGAGATTT TCAGATTACAGCTTCAGGACAATATGGACAGTGGGCCCCAAAGCTGG CCAGACTTCATTATTCCGGATCAATCAATGCCTGGAGCACCAAGGAG CCCTTTTCTTGGATCAAGGTGGATCTGTTGGCACCAATGATTATTCAC GGCATCAAGACCCAGGGTGCCCGTCAGAAGTTCTCCAGCCTCTACAT CTCTCAGTTTATCATCATGTATAGTCTTGATGGGAAGAAGTGGCAGA CTTATCGAGGAAATTCCACTGGAACCTTAATGGTCTTCTTTGGCAATG TGGATTCATCTGGGATAAAACACAATATTTTTAACCCTCCAATTATTG CTCGATACATCCGTTTGCACCCAACTCATTATAGCATTCGCAGCACTC TTCGCATGGAGTTGATGGGCTGTGATTTAAATAGTTGCAGCATGCCAT TGGGAATGGAGAGTAAAGCAATATCAGATGCACAGATTACTGCTTCA TCCTACTTTACCAATATGTTTGCCACCTGGTCTCCTTCAAAAGCTCGA CTTCACCTCCAAGGGAGGAGTAATGCCTGGAGACCTCAGGTGAATAA TCCAAAAGAGTGGCTGCAAGTGGACTTCCAGAAGACAATGAAAGTCA CAGGAGTAACTACTCAGGGAGTAAAATCTCTGCTTACCAGCATGTAT GTGAAGGAGTTCCTCATCTCCAGCAGTCAAGATGGCCATCAGTGGAC TCTCTTTTTTCAGAATGGCAAAGTAAAGGTTTTTCAGGGAAATCAAGA CTCCTTCACACCTGTGGTGAACTCTCTAGACCCACCGTTACTGACTCG CTACCTTCGAATTCACCCCCAGAGTTGGGTGCACCAGATTGCCCTGAG GATGGAGGTTCTGGGCTGCGAGGCACAGGACCTCTACTGAGGGTGGC CACTGCAGCACCTGCCACTGCCGTCACCTCTCCCTCAGCTCCAGG GCAGTGTCCCTCCCTGGCTTGCCTTCTACCTTTGTGCTAAATCCTAGC AGACACTGCCTTGAAGCCTCCTGAATTAACTATCATCAGTCCTGCATT TCTTTGGTGGGGGCCAGGAGGGTGCATCCAATTTAACTTAACTCTTA CCTATTTCTGCAGCTGCTCCCAGATTACTCCTTCCTTCCAATATAACT AGGCAAAAAGAAGTGAGGAGAAACCTGCATGAAAGCATTCTTCCCTG AAAAGTTAGGCCTCTCAGAGTCACCACTTCCTCTGTTGTAGAAAAACT ATGTGATGAAAACTTTGAAAAAGATATTTATGATGTTAACATTTCAGGT TAAGCCTCATACGTTTAAAATAAAACTCTCAGTTGTTTATTATCCTGA TCAAGCATGGAACAAAGCATGTTTCAGGATCAGATCAATACAATCTT GGAGTCAAAAGGCAAATCATTTGGACAATCTGCAAAATGGAGAGAA TACAATAACTACTACAGTAAAGTCTGTTTCTGCTTCCTTACACATAGA TATAATTATGTTATTTAGTCATTATGAGGGGCACATTCTTATCTCCAA AACTAGCATTCTTAAACTGAGAATTATAGATGGGGTTCAAGAATCCC TAAGTCCCCTGAAATTATATAAGGCATTCTGTATAAATGCAAATGTGC ATTTTTCTGACGAGTGTCCATAGATATAAAGCCATTTGGTCTTAATTCT GACCAATAAAAAAATAAGTCAGGAGGATGCAATTGTTGAAAGCTTTG AAATGATGA

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Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe Cys Phe Ser Ala Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser Trp Asp Tyr Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln Ala Glu Val Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asp Ser Pro Ser Phe Ile Gln Île Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Ser Arg His Arg Ser Thr Arg Gln Lys Gln Phe Asn Ala Thr Thr Ile Pro Glu Asn Asp Ile Glu Lys Thr Asp Pro Trp

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Phe Ala His Arg Thr Pro Met Pro Lys Ile Gln Asn Val Ser Ser Ser Asp Leu Leu Met Leu Leu Arg Gin Ser Pro Thr Pro His Gly Leu Ser Leu Ser Asp Leu Gln Glu Ala Lys Tyr Glu Thr Phe Ser Asp Asp Pro Ser Pro Gly Ala Ile Asp Ser Asn Asn Ser Leu Ser Glu Met Thr His Phe Arg Pro Gln Leu His His Ser Gly Asp Met Val Phe Thr Pro Glu Ser Gly Leu Gln Leu Arg Leu Asn Glu Lys Leu Gly Thr Thr Ala Ala Thr Glu Leu Lys Lys Leu Asp Phe Lys Val Ser Ser Thr Ser Asn Asn Leu Ile Ser Thr Ile Pro Ser Asp Asn Leu Ala Ala Gly Thr Asp Asn Thr Ser Ser Leu Gly Pro Pro Ser Met Pro Val His Tyr Asp Ser Gln Leu Asp Thr Thr Leu Phe Gly Lys Lys Ser Ser Pro Leu Thr Glu Ser Gly Gly Pro Leu Ser Leu Ser Glu Glu Asn Asn Asp Ser Lys Leu Leu Glu Ser Gly Leu Met Asn Ser Gln Glu Ser Ser Trp Gly Lys Asn Val Ser Ser Thr Glu Ser Gly Arg Leu Phe Lys Gly Lys Arg Ala His Gly Pro Ala Leu Leu Thr Lys Asp Asn Ala Leu Phe Lys Val Ser Ile Ser Leu Leu Lys Thr Asn Lys Thr Ser Asn Asn Ser Ala Thr Asn Arg Lys Thr His Ile Asp Gly Pro Ser Leu Leu Ile Glu Asn Ser Pro Ser Val Trp Gln Asn Ile Leu Glu Ser Asp Thr Glu Phe Lys Lys Val Thr Pro Leu Ile His Asp Arg Met Leu Met Asp Lys Asn Ala Thr Ala Leu Arg Leu Asn His Met Ser Asn Lys Thr Thr Ser Ser Lys Asn Met Glu Met Val Gln Gln Lys Lys Glu Gly Pro Ile Pro Pro Asp Ala Gln Asn Pro Asp Met Ser Phe Phe Lys Met Leu Phe Leu Pro Glu Ser Ala Arg Trp Ile Gln Arg Thr His Gly Lys Asn Ser Leu Asn Ser Gly Gln Gly Pro Ser Pro Lys Gln Leu Val Ser Leu Gly Pro Glu Lys Ser Val Glu Gly Gln Asn Phe Leu Ser Glu Lys Asn Lys Val Val Val Gly Lys Gly Glu Phe Thr Lys Asp Val Gly Leu Lys Glu Met Val Phe Pro Ser Ser Arg Asn Leu Phe Leu Thr Asn Leu Asp Asn Leu His Glu Asn Asn Thr His Asn Gln Glu Lys Lys Ile Gln Glu Glu Ile Glu Lys Lys Glu Thr Leu Ile Gln Glu Asn Val Val Leu Pro Gln Ile His Thr Val Thr Gly Thr Lys Asn Phe Met Lys Asn Leu Phe Leu Leu Ser Thr Arg Gln Asn Val Glu Gly Ser Tyr Asp Gly Ala Tyr Ala Pro Val Leu Gln Asp Phe Arg Ser Leu Asn Asp Ser Thr Asn Arg Thr Lys Lys His Thr Ala His Phe Ser Lys Lys Gly Glu Glu Glu Asn Leu Glu Gly Leu Gly Asn Gln Thr Lys Gln Ile Val Glu Lys Tyr Ala Cys Thr Thr Arg Ile Ser Pro Asn Thr Ser Gln Gln Asn Phe Val Thr Gln Arg Ser Lys Arg Ala Leu Lys Gln Phe Arg Leu Pro Leu Glu Glu Thr Glu Leu Glu Lys Arg Ile Ile Val Asp Asp Thr Ser Thr Gln Trp Ser Lys Asn Met Lys His Leu Thr Pro Ser Thr Leu Thr Gln Ile Asp Tyr Asn Glu Lys Glu Lys Gly Ala Ile Thr Gln Ser Pro Leu Ser Asp Cys Leu Thr Arg Ser His Ser Ile Pro Gln Ala Asn Arg Ser Pro Leu Pro Ile Ala Lys Val Ser Ser Phe Pro Ser Ile Arg Pro Ile Tyr Leu Thr Arg Val Leu Phe Gln Asp Asn Ser Ser His Leu Pro Ala Ala Ser Tyr Arg Lys Lys Asp Ser Gly Val Gln Glu Ser Ser His Phe Leu Gln Gly Ala Lys Lys Asn Asn Leu Ser Leu Ala Ile Leu Thr Leu Glu Met Thr Gly Asp Gln Arg Glu Val Gly Ser Leu Gly Thr Ser Ala Thr Asn Ser Val Thr Tyr Lys Lys Val Glu Asn Thr Val Leu Pro Lys Pro Asp Leu Pro Lys Thr Ser Gly Lys Val Glu Leu Leu Pro Lys Val His Ile Tyr Gln Lys Asp Leu Phe Pro Thr Glu Thr Ser Asn Gly Ser Pro Gly His Leu Asp Leu Val Glu Gly Ser Leu

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Leu Gln Gly Thr Glu Gly Ala Ile Lys Trp Asn Glu Ala Asn Arg Pro Gly Lys Val Pro Phe Leu Arg Val Ala Thr Glu Ser Ser Ala Lys Thr Pro Ser Lys Leu Leu Asp Pro Leu Ala Trp Asp Asn His Tyr Gly Thr Gln Ile Pro Lys Glu Glu Trp Lys Ser Gln Glu Lys Ser Pro Glu Lys Thr Ala Phe Lys Lys Lys Asp Thr Ile Leu Ser Leu Asn Ala Cys Glu Ser Asn His Ala Ile Ala Ala Ile Asn Glu Gly Gln Asn Lys Pro Glu Ile Glu Val Thr Trp Ala Lys Gln Gly Arg Thr Glu Arg Leu Cys Ser Gln Asn Pro Pro Val Leu Lys Arg His Gln Arg Glu Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln Glu Glu Ile Asp Tyr Asp Asp Thr Ile Ser Val Glu Met Lys Lys Glu Asp Phe Asp Ile Tyr Asp Glu As Ser Phe Gln Lys Lys Thr Arg His Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp Asp Tyr Gly Met Ser Ser Ser Pro His Val Leu Arg Asn Arg Ala Gln Ser Gly Ser Val Pro Gln Phe Lys Lys Val Val Phe Gln Glu Phe Thr Asp Gly Ser Phe Thr Gln Pro Leu Tyr Arg Gly Glu Leu Asn Glu His Leu Gly Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Arg Asn Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Glu Glu Asp Gln Arg Gln Gly Ala Glu Pro Arg Lys Asn Phe Val Lys Pro Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val Gln His His Met Ala Pro Thr Lys Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly Pro Leu Leu Val Cys His Thr Asn Thr Leu Asn Pro Ala His Gly Arg Gln Val Thr Val Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp Tyr Phe Thr Glu Asn Met Glu Arg Asn Cys Arg Ala Pro Cys Asn Ile Gln Met Glu Asp Pro Thr Phe Lys Glu Asn Tyr Arg Phe His Ala Ile Asn Gly Tyr Ile Met Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asp Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn Ile His Ser Ile His Phe Ser Gly His Val Phe Thr Val Arg Lys Lys Glu Glu Tyr Lys Met Ala Leu Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr Val Glu Met Leu Pro Ser Lys Ala Gly Ile Trp Arg Val Glu Cys Leu Ile Gly Glu His Leu His Ala Gly Met Ser Thr Leu Phe Leu Val Tyr Ser Asn Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Ile Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His Gln Trp Thr Leu Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp Ser Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr Leu Arg Ile His

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Pro Gl
n Ser Trp Val His Gl
n Ile Ala Leu Arg Met Glu Val Leu Gly Cys Glu Ala Gl
n Asp Leu Tyr

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FIG. 66A

TCCACCTGTCCCCGCAGCGCCGGCTCGCGCCCTCCTGCCGCAGCCACC GAGCCGCCGTCTAGCGCCCCGACCTCGCCACCATGAGAGCCCTGCTG GCGCGCCTGCTTCTCTGCGTCCTGGTCGTGAGCGACTCCAAAGGCAGC AATGAACTTCATCAAGTTCCATCGAACTGTGACTGTCTAAATGGAGGA ACATGTGTGTCCAACAAGTACTTCTCCAACATTCACTGGTGCAACTGC CCAAAGAAATTCGGAGGGCAGCACTGTGAAATAGATAAGTCAAAAAC CTGCTATGAGGGGAATGGTCACTTTTACCGAGGAAAGGCCAGCACTG ACACCATGGGCCGGCCCTGCCTGCCTGGAACTCTGCCACTGTCCTTC AGCAAACGTACCATGCCCACAGATCTGATGCTCTTCAGCTGGGCCTGG GGAAACATAATTACTGCAGGAACCCAGACAACCGGAGGCGACCCTGG TGCTATGTGCAGGTGGGCCTAAAGCCGCTTGTCCAAGAGTGCATGGT GCATGACTGCGCAGATGGAAAAAAGCCCTCCTCCTCCAGAAGAAT TAAAATTTCAGTGTGGCCAAAAGACTCTGAGGCCCCGCTTTAAGATTA TTGGGGGAGAATTCACCACCATCGAGAACCAGCCCTGGTTTGCGGCC ATCTACAGGAGGCACCGGGGGGGGCTCTGTCACCTACGTGTGTGGAGG CAGCCTCATCAGCCCTTGCTGGGTGATCAGCGCCACACACTGCTTCAT TGATTACCCAAAGAAGGAGGACTACATCGTCTACCTGGGTCGCTCAA GGCTTAACTCCAACACGCAAGGGGAGATGAAGTTTGAGGTGGAAAAC CTCATCCTACACAAGGACTACAGCGCTGACACGCTTGCTCACCACAAC GACATTGCCTTGCAAGATCCGTTCCAAGGAGGCAGGTGTGCGCA GCCATCCGGACTATACAGACCATCTGCCTGCCCTCGATGTATAACGA TCCCCAGTTTGGCACAAGCTGTGAGATCACTGGCTTTGGAAAAGAGA ATTCTACCGACTATCTCTATCCGGAGCAGCTGAAGATGACTGTTGTGA AGCTGATTTCCCACCGGGAGTGTCAGCAGCCCCACTACTACGGCTCTG AAGTCACCACCAAAATGCTGTGTGCTGCTGACCCACAGTGGAAAACA GATTCCTGCCAGGGAGACTCAGGGGGACCCCTCGTCTGTTCCCTCCAA GGCCGCATGACTTTGACTGGAATTGTGAGCTGGGGCCGTGGATGTGC CCTGAAGGACAAGCCAGGCGTCTACACGAGAGTCTCACACTTCTTAC GGGTCCCCAGGGAGGAAACGGGCACCACCCGCTTTCTTGCTGGTTGTC ATTTTTGCAGTAGAGTCATCTCCATCAGCTGTAAGAAGAGACTGGGA AGAT

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FIG. 66B

Met Arg Ala Leu Leu Ala Arg Leu Leu Cys Val Leu Val Val Ser Asp Ser Lys Gly Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp Cys Leu Asn Gly Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile His Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile Asp Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly Lys Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser Ala Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg Arg Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln Glu Cys Met Val His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro Pro Glu Glu Leu Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg Phe Lys Ile Ile Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn Leu Île Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu

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FIG.67A

TCCTGCACAGGCAGTGCCTTGAAGTGCTTCTTCAGAGACCTTTCTTCA TAGACTACTTTTTTTTTTTAAGCAGCAAAAGGAGAAAATTGTCATCA AGGATATTCCAGATTCTTGACAGCATTCTCGTCATCTCTGAGGACATC ACCATCATCTCAGGATGAGGGGCATGAAGCTGCTGGGGGGCGCTGCTG GCACTGGCGGCCCTACTGCAGGGGGCCGTGTCCCTGAAGATCGCAGC CTTCAACATCCAGACATTTGGGGAGACCAAGATGTCCAATGCCACCCT CGTCAGCTACATTGTGCAGATCCTGAGCCGCTATGACATCGCCCTGGT CCAGGAGGTCAGAGACAGCCACCTGACTGCCGTGGGGAAGCTGCTGG ACAACCTCAATCAGGATGCACCAGACACCTATCACTACGTGGTCAGT GAGCCACTGGGACGGAACAGCTATAAGGAGCGCTACCTGTTCGTGTA CAGGCCTGACCAGGTGTCTGCGGTGGACAGCTACTACTACGATGATG GTCAGGTTCTCCCCGGTTCACAGAGGTCAGGGAGTTTGCCATTGTT CCCCTGCATGCGGCCCCGGGGGACGCAGTAGCCGAGATCGACGCTCT CTATGACGTCTACCTGGATGTCCAAGAGAAATGGGGCTTGGAGGACG TCATGTTGATGGGCGACTTCAATGCGGGCTGCAGCTATGTGAGACCCT CCCAGTGGTCATCCATCCGCCTGTGGACAAGCCCCACCTTCCAGTGGC TGATCCCCGACAGCGCTGACACCACAGCTACACCCACGCACTGTGCCT ATGACAGGATCGTGGTTGCAGGGATGCTGCTCCGAGGCGCCGTTGTTC CCGACTCGGCTCTTCCCTTTAACTTCCAGGCTGCCTATGGCCTGAGTG ACCAACTGGCCCAAGCCATCAGTGACCACTATCCAGTGGAGGTGATG CTGAAGTGAGCAGCCCTCCCCACACCAGTTGAACTGCAG

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FIG. 67B

Met Arg Gly Met Lys Leu Leu Gly Ala Leu Leu Ala Leu Ala Ala Leu Leu Gln Gly Ala Val Ser Leu Lys Ile Ala Ala Phe Asn Ile Gln Thr Phe Gly Glu Thr Lys Met Ser Asn Ala Thr Leu Val Ser Tyr Ile Val Gln Ile Leu Ser Arg Tyr Asp Ile Ala Leu Val Gln Glu Val Arg Asp Ser His Leu Thr Ala Val Gly Lys Leu Leu Asp Asn Leu Asn Gln Asp Ala Pro Asp Thr Tyr His Tyr Val Val Ser Glu Pro Leu Gly Arg Asn Ser Tyr Lys Glu Arg Tyr Leu Phe Val Tyr Arg Pro Asp Gln Val Ser Ala Val Asp Ser Tyr Tyr Asp Asp Gly Cys Glu Pro Cys Gly Asn Asp Thr Phe Asn Arg Glu Pro Ala Ile Val Arg Phe Phe Ser Arg Phe Thr Glu Val Arg Glu Phe Ala Ile Val Pro Leu His Ala Ala Pro Gly Asp Ala Val Ala Glu Ile Asp Ala Leu Tyr Asp Val Tyr Leu Asp Val Gln Glu Lys Trp Gly Leu Glu Asp Val Met Leu Met Gly Asp Phe Asn Ala Gly Cys Ser Tyr Val Arg Pro Ser Gln Trp Ser Ser Ile Arg Leu Trp Thr Ser Pro Thr Phe Gln Trp Leu Ile Pro Asp Ser Ala Asp Thr Thr Ala Thr Pro Thr His Cys Ala Tyr Asp Arg Ile Val Ala Gly Met Leu Arg Gly Ala Val Val Pro Asp Ser Ala Leu Pro Phe Asn Phe Gln Ala Ala Tyr Gly Leu Ser Asp Gln Leu Ala Gln Ala Ile Ser Asp His Tyr Pro Val Glu Val Met Leu Lys

FIG. 68A

FIG. 68B

Met Ala Leu Trp Met Arg Leu Leu Pro Leu Leu Ala Leu Leu Ala Leu Trp Gly Pro Asp Pro Ala Ala Ala Phe Val Asn Gln His Leu Cys Gly Ser His Leu Val Glu Ala Leu Tyr Leu Val Cys Gly Glu Arg Gly Phe Phe Tyr Thr Pro Lys Thr Arg Arg Glu Ala Glu Asp Leu Gln Val Gly Gln Val Glu Leu Gly Gly Gly Pro Gly Ala Gly Ser Leu Gln Pro Leu Ala Leu Glu Gly Ser Leu Gln Lys Arg Gly Ile Val Glu Gln Cys Cys Thr Ser Ile Cys Ser Leu Tyr Gln Leu Glu Asn Tyr Cys Asn

FIG. 69A

ATGGGAGGTTGGTCTTCCAAACCTCGACAAGGCATGGGGACGAATCT TTCTGTTCCCAATCCTCTGGGATTCTTTCCCGATCACCAGTTGGACCCT GCGTTCGGAGCCAACTCAAACAATCCAGATTGGGACTTCAACCCCAA CAAGGATCACTGGCCAGAGGCAATCAAGGTAGGAGCGGGAGACTTC GGGCCAGGGTTCACCCCACCACACGGCGTCTTTTGGGGTGGAGCCC TCAGGCTCAGGGCATATTGACAACAGTGCCAGCAGCGCCTCCTCCTG TTTCCACCAATCGGCAGTCAGGAAGACAGCCTACTCCCATCTCTCCAC CTCTAAGAGACAGTCATCCTCAGGCCATGCAGTGGAACTCCACAACA TTCCACCAAGCTCTGCTAGATCCCAGAGTGAGGGGCCTATATTTTCCT GCTGGTGGCTCCAGTTCCGGAACAGTAAACCCTGTTCCGACTACTGTC TCACCCATATCGTCAATCTTCTCGAGGACTGGGGACCCTGCACCGAAC ATGGAGAGCACAACATCAGGATTCCTAGGACCCCTGCTCGTGTTACA GGCGGGGTTTTTCTTGTTGACAAGAATCCTCACAATACCACAGAGTCT AGACTCGTGGTGGACTTCTCTCAATTTTCTAGGGGGAGCACCCACGTG TTGTCCTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTTT ATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTGTTGGTTC TTCTGGACTACCAAGGTATGTTGCCCGTTTGTCCTCTACTTCCAGGAA CATCAACTACCAGCACGGGACCATGCAAGACCTGCACGATTCCTGCT CAAGGAACCTCTATGTTTCCCTCTTGTTGCTGTACAAAACCTTCGGAC GGAAACTGCACTTGTATTCCCATCCCATCATCCTGGGCTTTCGCAAGA TTCCTATGGGAGTGGGCCTCAGTCCGTTTCTCCTGGCTCAGTTTACTA GTGCCATTTGTTCAGTGGTTCGCAGGGCTTTCCCCCACTGTTTGGCTTT CAGTTATATGGATGATGTGGTATTGGGGGCCAAGTCTGTACAACATCT TGAGTCCCTTTTTACCTCTATTACCAATTTTCTTTTGTCTTTGGGTATAC **ATTTGA**

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FIG. 69B

Met Gly Gly Trp Ser Ser Lys Pro Arg Gln Gly Met Gly Thr Asn Leu Ser Val Pro Asn Pro Leu Gly Phe Phe Pro Asp His Gln Leu Asp Pro Ala Phe Gly Ala Asn Ser Asn Asn Pro Asp Trp Asp Phe Asn Pro Asn Lys Asp His Trp Pro Glu Ala Ile Lys Val Gly Ala Gly Asp Phe Gly Pro Gly Phe Thr Pro Pro His Gly Gly Leu Leu Gly Trp Ser Pro Gln Ala Gln Gly Ile Leu Thr Thr Val Pro Ala Ala Pro Pro Pro Val Ser Thr Asn Arg Gln Ser Gly Arg Gln Pro Thr Pro Ile Ser Pro Pro Leu Arg Asp Ser His Pro Gln Ala Met Gln Trp Asn Ser Thr Thr Phe His Gln Ala Leu Leu Asp Pro Arg Val Arg Gly Leu Tyr Phe Pro Ala Gly Gly Ser Ser Ser Gly Thr Val Asn Pro Val Pro Thr Thr Val Ser Pro Ile Ser Ser Ile Phe Ser Arg Thr Gly Asp Pro Ala Pro Asn Met Glu Ser Thr Thr Ser Gly Phe Leu Gly Pro Leu Leu Val Leu Gln Ala Gly Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile Pro Gln Ser Leu Asp Ser Trp Trp Thr Ser Leu Asn Phe Leu Gly Gly Ala Pro Thr Cys Pro Gly Gln Asn Ser Gln Ser Pro Thr Ser Asn His Ser Pro Thr Ser Cys Pro Pro Ile Cys Pro Gly Tyr Arg Trp Met Cys Leu Arg Arg Phe Ile Ile Phe Leu Phe Ile Leu Leu Cys Leu Ile Phe Leu Leu Val Leu Leu Asp Tyr Gln Gly Met Leu Pro Val Cys Pro Leu Leu Pro Gly Thr Ser Thr Thr Ser Thr Gly Pro Cys Lys Thr Cys Thr Ile Pro Ala Gln Gly Thr Ser Met Phe Pro Ser Cys Cys Cys Thr Lys Pro Ser Asp Gly Asn Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp Ala Phe Ala Arg Phe Leu Trp Glu Trp Ala Ser Val Arg Phe Ser Trp Leu Ser Leu Leu Val Pro Phe Val Gln Trp Phe Ala Gly Leu Ser Pro Thr Val Trp Leu Ser Val Ile Trp Met Met Trp Tyr Trp Gly Pro Ser Leu Tyr Asn Ile Leu Ser Pro Phe Leu Pro Leu Pro Ile Phe Phe Cys Leu Trp Val Tyr Ile

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FIG. 70A

CGAACCACTCAGGGTCCTGTGGACAGCTCACCTAGCTGCAATGGCTA CCTGGCTTCAAGAGGGCAGTGCCTTCCCAACCATTCCCTTATCCAGGC CTTTTGACAACGCTATGCTCCGCGCCCCATCGTCTGCACCAGCTGGCCT TTGACACCTACCAGGAGTTTGAAGAAGCCTATATCCCAAAGGAACAG AAGTATTCATTCCTGCAGAACCCCCAGACCTCCCTCTGTTTCTCAGAG TCTATTCCGACACCCTCCAACAGGGAGGAAACACAACAGAAATCCAA CCTAGAGCTGCTCCGCATCTCCCTGCTGCTCATCCAGTCGTGGCTGGA GCCCGTGCAGTTCCTCAGGAGTGTCTTCGCCAACAGCCTGGTGTACGG CGCCTCTGACAGCAACGTCTATGACCTCCTAAAGGACCTAGAGGAAG GCATCCAAACGCTGATGGGGAGGCTGGAAGATGGCAGCCCCCGGACT GGGCAGATCTTCAAGCAGACCTACAGCAAGTTCGACACAAACTCACA CAACGATGACGCACTACTCAAGAACTACGGGCTGCTCTACTGCTTCAG GAAGGACATGGCAAGGTCGAGACATTCCTGCGCATCGTGCAGTGCCG CTCTGTGGAGGGCAGCTGTGGCTTCTAGCTGCCCGGGTGGCATCCCTG TGACCCCTCCCCAGTGCCTCTCCTGGCCCTGGAAGTTGCCACTCCAGT GCCCACCAGCCTTGTCCTAATAAAATTÄAGTTGCATC

FIG. 70B

Met Ala Thr Gly Ser Arg Thr Ser Leu Leu Leu Ala Phe Gly Leu Leu Cys Leu Pro Trp Leu Gln Glu Gly Ser Ala Phe Pro Thr Ile Pro Leu Ser Arg Pro Phe Asp Asn Ala Met Leu Arg Ala His Arg Leu His Gln Leu Ala Phe Asp Thr Tyr Gln Glu Phe Glu Glu Ala Tyr Ile Pro Lys Glu Gln Lys Tyr Ser Phe Leu Gln Asn Pro Gln Thr Ser Leu Cys Phe Ser Glu Ser Ile Pro Thr Pro Ser Asn Arg Glu Glu Thr Gln Gln Lys Ser Asn Leu Glu Leu Leu Arg Ile Ser Leu Leu Ile Gln Ser Trp Leu Glu Pro Val Gln Phe Leu Arg Ser Val Phe Ala Asn Ser Leu Val Tyr Gly Ala Ser Asp Ser Asn Val Tyr Asp Leu Leu Lys Asp Leu Glu Glu Gly Ile Gln Thr Leu Met Gly Arg Leu Glu Asp Gly Ser Pro Arg Thr Gly Gln Ile Phe Lys Gln Thr Tyr Ser Lys Phe Asp Thr Asn Ser His Asn Asp Asp Ala Leu Leu Lys Asn Tyr Gly Leu Leu Tyr Cys Phe Arg Lys Asp Met Asp Lys Val Glu Thr Phe Leu Arg Ile Val Gln CysArg Ser Val Glu Gly Ser Cys Gly Phe

FIG. 71A

ATGGCGCCGTCGCCGTCTGGGCCGCCGCTCGGACTGGAGCT CTGGGCTGCGCCACGCCTTGCCCGCCCAGGTGGCATTTACACCCTA CGCCCGGAGCCCGGGAGCACATGCCGGCTCAGAGAATACTATGACC AGACAGCTCAGATGTGCTGCAGCAAATGCTCGCCGGGCCAACATGCA AAAGTCTTCTGTACCAAGACCTCGGACACCGTGTGTGACTCCTGTGAG GACAGCACATACACCCAGCTCTGGAACTGGGTTCCCGAGTGCTTGAG CTGTGGCTCCCGCTGTAGCTCTGACCAGGTGGAAACTCAAGCCTGCAC TCGGGAACAGAACCGCATCTGCACCTGCAGGCCCGGCTGGTACTGCG CGCTGAGCAAGCAGGAGGGGTGCCGGCTGTGCGCGCAAG TGCCGCCCGGGCTTCGCCGTGGCCAGACCAGGAACTGAAACATCAGA CGTGGTGTGCAAGCCCTGTGCCCCGGGGACGTTCTCCAACACGACTTC ATCCACGGATATTTGCAGGCCCCACCAGATCTGTAACGTGGTGGCCAT CCCTGGGAATGCAAGCATGGATGCAGTCTGCACGTCCCCCA ACACGATCCCAACACGCAGCCAACTCCAGAACCCAGCACTGCTCC AAGCACCTCCTTCCTGCTCCCAATGGGCCCCAGCCCCCAGCTGAAGG GAGCACTGGCGACTTCGCTCTTCCAGTTGGACTGATTGTGGGTGTGAC AGCCTTGGGTCTACTAATAATAGGAGTGGTGAACTGTGTCATCATGAC CCAGGTGAAAAAGAAGCCCTTGTGCCTGCAGAGAGAAGCCAAGGTGC CTCACTTGCCTGCCGATAAGGCCCGGGGTACACAGGGCCCCGAGCAG CAGCACCTGCTGATCACAGCGCCGAGCTCCAGCAGCAGCTCCCTGGA GAGCTCGGCCAGTGCGTTGGACAGAAGGGCGCCCACTCGGAACCAGC CACAGGCACCAGGCGTGGAGGCCAGTGGGGCCCGGGGC CAGCACCGGGAGCTCAGATTCTTCCCCTGGTGGCCATGGGACCCAGG TCAATGTCACCTGCATCGTGAACGTCTGTAGCAGCTCTGACCACAGCT CACAGTGCTCCCCAAGCCAGCTCCACAATGGGAGACACAGATTCC AGCCCTCGGAGTCCCCGAAGGACGAGCAGGTCCCCTTCTCCAAGGA GGAATGTGCCTTTCGGTCACAGCTGGAGACGCCAGAGACCCTGCTGG GGAGCACCGAAGAGAGCCCCTGCCCCTTGGAGTGCCTGATGCTGGG ATGAAGCCCAGTTAACCAGGCCGGTGTGGGCTGTGTCGTAGCCAAGG TGGGCTGAGCCCTGGCAGGATGACCCTGCGAAGGGGCCCTGGTCCTT **CCAGGC**

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FIG. 71B

Met Ala Pro Val Ala Val Trp Ala Ala Leu Ala Val Gly Leu Glu Leu Trp Ala Ala Ala His Ala Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val Ala Arg Pro Gly Thr Glu Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val Val Ala Ile Pro Gly Asn Ala Ser Met Asp Ala Val Cys Thr Ser Thr Ser Pro Thr Arg Ser Met Ala Pro Gly Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser Gln His Thr Gln Pro Thr Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser Phe Leu Leu Pro Met Gly Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly Asp Phe Ala Leu Pro Val Gly Leu Ile Val Gly Val Thr Ala Leu Gly Leu Leu Ile Ile Gly Val Val Asn Cys Val Ile Met Thr Gln Val Lys Lys Pro Leu Cys Leu Gln Arg Glu Ala Lys Val Pro His Leu Pro Ala Asp Lys Ala Arg Gly Thr Gln Gly Pro Glu Gln Gln His Leu Leu Ile Thr Ala Pro Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala Ser Ala Leu Asp Arg Arg Ala Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly Val Glu Ala Ser Gly Ala Gly Glu Ala Arg Ala Ser Thr Gly Ser Ser Asp Ser Ser Pro Gly Gly His Gly Thr Gln Val Asn Val Thr Cys Ile Val Asn Val Cys Ser Ser Ser Asp His Ser Ser Gln Cys Ser Ser Gln Ala Ser Ser Thr Met Gly Asp Thr Asp Ser Ser Pro Ser Glu Ser Pro Lys Asp Glu Gln Val Pro Phe Ser Lys Glu Glu Cys Ala Phe Arg Ser Gln Leu Glu Thr Pro Glu Thr Leu Leu Gly Ser Thr Glu Glu Lys Pro Leu Pro Leu Gly Val Pro Asp Ala Gly Met Lys Pro Ser

FIG. 72A

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Asn Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Thr Thr Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys

FIG. 72B

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Lys Asp Thr Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser

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FIG. 73A

Gln Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser Gly Met Ser Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Ala Leu Glu Trp Leu Ala Asp Ile Trp Trp Asp Asp Lys Lys Asp Tyr Asn Pro Ser Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Val Leu Lys Val Thr Asn Met Asp Pro Ala Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Ser Met Ile Thr Asn Trp Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser

FIG. 73B

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Cys Gln Leu Ser Val Gly Tyr Met His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Trp Ile Tyr Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Phe Gln Gly Ser Gly Tyr Pro Phe Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

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FIG. 74A

GACATCTTGCTGACTCAGTCTCCAGCCATCCTGTCTGAGTCCAGGA
GAAAGAGTCAGTTTCTCCTGCAGGGCCAGTCAGTTCGTTGGCTCAAGC
ATCCACTGGTATCAGCAAAGAACAAATGGTTCTCCAAGGCTTCTCATA
AAGTATGCTTCTGAGTCTATGTCTGGGATCCCTTCCAGGTTTAGTGGC
AGTGGATCAGGGACAGATTTTACTCTTAGCATCAACACTGTGGAGTCT
GAAGATATTGCAGATTATTACTGTCAACAAAGTCATAGCTGGCCATTC
ACGTTCGGCTCGGGGACAAATTTGGAAGTAAAAGAAGTGAAGCTTGA
GGAGTCTGGAGGAGGCTTGGTGCAACCTGGAGGATCCATGAAACTCT
CCTGTGTTGCCTCTGGATTCATTTTCAGTAACCACTGGATGAACTGGG
TCCGCCAGTCTCCAGAGAAGGGGCTTGAGTGGGTTGCTGAAATTAGA
TCAAAATCTATTAATTCTGCAACACATTATGCGGAGTCTGTGAAAGGG
AGGTTCACCATCTCAAGAGATGATTCCAAAAAGTGCTGTCTACCTGCAA
ATGACCGACTTAAGAACTGAAGACACTGGCGTTTATTACTGTTCCAGG
AATTACTACGGTAGTACCTACGACTACTGGGGCCAAGGCACCACTCTC
ACAGTCTCC

FIG. 74B

Asp IIe Leu Leu Thr Gln Ser Pro Ala IIe Leu Ser Val Ser Pro Gly Glu Arg Val Ser Phe Ser Cys Arg Ala Ser Gln Phe Val Gly Ser Ser IIe His Trp Tyr Gln Gln Arg Thr Asn Gly Ser Pro Arg Leu Leu IIe Lys Tyr Ala Ser Glu Ser Met Ser Gly IIe Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Ser IIe Asn Thr Val Glu Ser Glu Asp IIe Ala Asp Tyr Tyr Cys Gln Gln Ser His Ser Trp Pro Phe Thr Phe Gly Ser Gly Thr Asn Leu Glu Val Lys Glu Val Lys Leu Glu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Met Lys Leu Ser Cys Val Ala Ser Gly Phe IIe Phe Ser Asn His Trp Met Asn Trp Val Arg Gln Ser Pro Glu Lys Gly Leu Glu Trp Val Ala Glu IIe Arg Ser Lys Ser IIe Asn Ser Ala Thr His Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr IIe Ser Arg Asp Asp Ser Lys Ser Ala Val Tyr LeuGln Met Thr Asp Leu Arg Thr Glu Asp Thr Gly Val Tyr Tyr Cys Ser Arg Asn Tyr Tyr Gly Ser Thr Tyr Asp Tyr Trp Gly Gln Gly Thr Thr Leu Thr Val Ser

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FIG. 75A

ATGGAGACAGACACTCCTGTTATGGGTGCTGCTGCTCTGGGTTCCA GGTTCCACTGGTGACGTCAGGCGAGGCCCCGGAGCCTGCGGGGCAG GGACGCCCAGCCCCACGCCCTGCGTCCCGGCCGAGTGCTTCGACC TGCTGGTCCGCCACTGCGTGGCCTGCGGGCTCCTGCGCACGCCGCGC CGAAACCGGCCGGGCCAGCAGCCCTGCGCCCAGGACGCCGCTGCAG CCGCAGGAGTCGGTGGCCGCGGGGGCCGGCGAGGCGGCGGTCGACA AAACTCACACATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGA CCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATC TCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGA AGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGCGTGGAGGTGC ATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTA CCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGG CAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCA TCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAG GTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGT CAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGT GGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACG CCTCCCGTGTTGGACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTC ACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTC CGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT CCCTGTCTCCCGGGAAATGA

FIG. 75B

Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro Gly Ser Thr Gly Asp Val Arg Arg Gly Pro Arg Ser Leu Arg Gly Arg Asp Ala Pro Ala Pro Thr Pro Cys Val Pro Ala Glu Cys Phe Asp Leu Leu Val Arg His Cys Val Ala Cys Gly Leu Leu Arg Thr Pro Arg Pro Lys Pro Ala Gly Ala Ser Ser Pro Ala Pro Arg Thr Ala Leu Gln Pro Gln Glu Ser Val Gly Ala Gly Ala Gly Glu Ala Ala Val Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys

FIG. 76

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Ile Val Lys Leu Leu Ile Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

FIG. 77

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Gly Pro Gly Thr Ser Val Arg Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Leu Ile Glu Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Thr Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Asp Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ala

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FIG. 78

Asp Ile Gln Met Thr Gln Thr Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Val Lys

FIG. 79

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Leu Ile Glu Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe Lys Gly Arg Val Thr Leu Thr Val Asp Glu Ser Thr Asn Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser

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FIG. 80

Asp Ile Gln Met Thr Gln Thr Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Val Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys

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FIG. 81

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Leu Ile Glu Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe Lys Gly Arg Val Thr Leu Thr Val Asp Glu Ser Thr Asn Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly

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FIG. 82A

FIG. 82B

Met Asp Phe Gln Val Gln Ile Ile Ser Phe Leu Leu Ile Ser Ala Ser Val Ile Met Ser Arg Gly Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Ile His Trp Phe Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Ser Asn Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

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FIG. 83A

FIG. 83B

Met Gly Trp Ser Leu Ile Leu Leu Phe Leu Val Ala Val Ala Thr Arg Val Leu Ser Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys Gln Thr Pro Gly Arg Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser Thr Tyr Tyr Gly Gly Asp Trp Tyr Phe Asn Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ala

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CAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTG ACGCAAATGGGCGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAG AGCTGGGTACGTCCTCACATTCAGTGATCAGCACTGAACACAGACCC GTCGACATGGGTTGGAGCCTCATCTTGCTCTTCCTTGTCGCTGTTGCTA CGCGTGTCGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCT CCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTC AAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGC CCTGACCAGCGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGG ACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGG CACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCA AGGTGGACAAGAAAGCAGAGCCCAAATCTTGTGACAAAACTCACACA ${\tt TGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTTC}$ CTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCT GAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGT CAAGTTCAACTGGTACGTGGACGCGTGGAGGTGCATAATGCCAAGA CAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGC GTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGACTACAA GTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCA TCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTG CCCCCATCCCGGGATGAGCTGACCAGGAACCAGGTCAGCCTGACCTG CCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGA GCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTG GACTCCGACGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAG AGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGA GGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGG TAAATGAGGATCCGTTAACGGTTACCAACTACCTAGACTGGATTCGTG ACAACATGCGGCCGTGATATCTACGTATGATCAGCCTCGACTGTGCCT CCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGGAAA TTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGGG TGGGGCAGGACAGCAAGGGGGGAGGATTGGGAAGACAATAGCAGGCA TGCTGGGGATGCGGTGGGCTCTATGGAACCAGCTGGGGCTCGACAGC GCTGGATCTCCCGATCCCCAGCTTTGCTTCTCAATTTCTTATTTGCATA ATGAGAAAAAAAGGAAAATTAATTTTAACACCAATTCAGTAGTTGAT TGAGCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACAGTGTTCTCT GCACAGATAAGGACAAACATTATTCAGAGGGAGTACCCAGAGCTGAG ACTCCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGAAATATGCTT GTCATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGGTAAGGGCC ATAAGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTCTGACATAG TTGTGTTGGGAGCTTGGATAGCTTGGACAGCTCAGG

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FIG. 84B

CAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTG ACGCAAATGGGCGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAG AGCTGGGTACGTCCTCACATTCAGTGATCAGCACTGAACACAGACCC GTCGACATGGGTTGGAGCCTCATCTTGCTCTTCCTTGTCGCTGTTGCTA CGCGTGTCGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCT CCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTC AAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGC CCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGG ACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGG CACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCA AGGTGGACAAGAAGCAGAGCCCAAATCTTGTGACAAAACTCACACA TGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTTC CTCTTCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCT GAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGT CAAGTTCAACTGGTACGTGGACGCGTGGAGGTGCATAATGCCAAGA CAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGC GTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGACTACAA GTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCA TCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTG CCCCATCCCGGGATGAGCTGACCAGGAACCAGGTCAGCCTGACCTG CCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGA GCAATGGCCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTG GACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAG AGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGA GGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGG TAAATGAGGATCCGTTAACGGTTACCAACTACCTAGACTGGATTCGTG ACAACATGCGGCCGTGATATCTACGTATGATCAGCCTCGACTGTGCCT CCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGGAAA TGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGCA TGCTGGGGATGCGGTGGGCTCTATGGAACCAGCTGGGGCTCGACAGC GCTGGATCTCCCGATCCCCAGCTTTGCTTCTCAATTTCTTATTTGCATA ATGAGAAAAAAGGAAAATTAATTTTAACACCAATTCAGTAGTTGAT TGAGCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACAGTGTTCTCT GCACAGATAAGGACAAACATTATTCAGAGGGAGTACCCAGAGCTGAG ACTCCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGAAATATGCTT GTCATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGGTAAGGGCC ATAAGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTCTGACATAG TTGTGTTGGGAGCTTGGATAGCTTGGACAGCTCAGG

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GCTGCGATTTCGCGCCAAACTTGACGGCAATCCTAGCGTGAAGGCTG GTAGGATTTTATCCCCGCTGCCATCATGGTTCGACCATTGAACTGCAT CGTCGCCGTGTCCCAAAATATGGGGATTGGCAAGAACGGAGACCTAC CCTGGCCTCCGCTCAGGAACGAGTTCAAGTACTTCCAAAGAATGACC ACAACCTCTTCAGTGGAAGGTAAACAGAATCTGGTGATTATGGGTAG GAAAACCTGGTTCTCCATTCCTGAGAACAATCGACCTTTAAAGGACA GAATTAATATAGTTCTCAGTAGAGAACTCAAAGAACCACCACGAGGA GCTCATTTCTTGCCAAAAGTTTGGATGATGCCTTAAGACTTATTGAA CAACCGGAATTGGCAAGTAAAGTAGACATGGTTTGGATAGTCGGAGG CAGTTCTGTTTACCAGGAAGCCATGAATCAACCAGGCCACCTTAGACT CTTTGTGACAAGGATCATGCAGGAATTTGAAAGTGACACGTTTTTCCC AGAAATTGATTTGGGGAAATATAAACTTCTCCCAGAATACCCAGGCG TCCTCTCTGAGGTCCAGGAGGAAAAAGGCATCAAGTATAAGTTTGAA GTCTACGAGAAGAAGACTAACAGGAAGATGCTTTCAAGTTCTCTGC TCCCCTCCTAAAGTCATGCATTTTTATAAGACCATGGGACTTTTGCTG TTGCCCCTCCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCAC TGTCCTTTCCTAATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAG AGGATTGGGAAGACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCT ATGGAACCAGCTGGGGCTCGAGCTACTAGCTTTGCTTCTCAATTTCTT ATTTGCATAATGAGAAAAAAGGAAAATTAATTTTAACACCAATTCA GTAGTTGATTGAGCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACA GTGTTCTCTGCACAGATAAGGACAAACATTATTCAGAGGGAGTACCC AGAGCTGAGACTCCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGA AATATGCTTGTCATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGG TAAGGGCCAATCTGCTCACACAGGATAGAGAGGGCAGGAGCCAGGG CAGAGCATATAAGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTC TGACATAGTTGTGTGGGAGCTTGGATCGATCCTCTATGGTTGAACAA GATGGATTGCACGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTATTC GGCTATGACTGGGCACAACAGACAATCGGCTGCTCTGATGCCGCCGT GTTCCGGCTGTCAGCGCAGGGGCGCCCGGTTCTTTTTGTCAAGACCGA CCTGTCCGGTGCCCTGAATGAACTGCAGGACGAGGCAGCGCGGCTAT CGTGGCTGGCCACGACGGCGTTCCTTGCGCAGCTGTGCTCGACGTTG TCACTGAAGCGGGAAGGGACTGGCTGCTATTGGGCGAAGTGCCGGGG CAGGATCTCCTGTCATCTCACCTTGCTCCTGCCGAGAAAGTATCCATC ATGGCTGATGCAATGCGGCGGCTGCATACGCTTGATCCGGCTACCTGC CCATTCGACCACCAAGCGAAACATCGCATCGAGCGAGCACGTACTCG GATGGAAGCCGGTCTTGTCGATCAGGATGATCTGGACGAAGAGCATC AGGGGCTCGCGCCAGCCGAACTGTTCGCCAGGCTCAAGGCGCGCATG CCCGACGCGAGGATCTCGTCGTGACCCATGGCGATGCCTGCTTGCCG

294/345 FIG. 84D

AATATCATGGTGGAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGC CGGCTGGGTGTGGCGACCGCTATCAGGACATAGCGTTGGCTACCCG TGATATTGCTGAAGAGCTTGGCGGCGAATGGGCTGACCGCTTCCTCGT GCTTTACGGTATCGCCGCTTCCCGATTCGCAGCGCATCGCCTTCTATC GCCTTCTTGACGAGTTCTTCTGAGCGGGACTCTGGGGTTCGAAATGAC CGACCAAGCGACCCCAACCTGCCATCACGAGATTTCGATTCCACCG CCGCCTTCTATGAAAGGTTGGGCTTCGGAATCGTTTTCCGGGACGCCG GCTGGATGATCCTCCAGCGCGGGGATCTCATGCTGGAGTTCTTCGCCC ACCCCAACTTGTTTATTGCAGCTTATAATGGTTACAAATAAAGCAATA GCATCACAAATTCACAAATAAAGCATTTTTTCACTGCATTCTAGTT GTGGTTTGTCCAAACTCATCAATCTATCTTATCATGTCTGGATCGCGG CCGCGATCCCGTCGAGAGCTTGGCGTAATCATGGTCATAGCTGTTTCC TGTGTGAAATTGTTATCCGCTCACAATTCCACACACACATACGAGCCGG AGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCAC ATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTC GTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTT TGCGTATTGGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTC GGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAA TACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGA GCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGC TGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATC GACGCTCAAGTCAGAGGTGGCGAAACCCCGACAGGACTATAAAGATAC CAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACC CTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTG GCGCTTTCTCAATGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTC GTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGAC CGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGA CACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAG AGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTA ACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGA AGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAA CAAACCACCGCTGGTAGCGGTGGTTTTTTTTTTTTTTCAAGCAGCAGCAGATT ACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTCTAC GGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGG TCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAA AATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTG ACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTC TATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTAC GATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGC GAGACCCACGCTCACCGCTCCAGATTTATCAGCAATAAACCAGCCA GCCGGAAGGCCCAGAAGTGGTCCTGCAACTTTATCCGCCTC

PCT/US02/32263

295/345 FIG. 84E

CAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGG
TGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAAC
GATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAAGCGGTT
AGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTG
TTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGC
CATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCAT
TCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAA
TACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAAGTGCTCATC
ATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTG
TTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCA
GCATCTTTTACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGG
CAAAATGCCGCAAAAAAAGGGAATAAGGGCGACACGGAAATGTTGAA
TACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTA
TTGTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAAATAAACA
AATAGGGGTTCCGCGCACATTTCCCCGAAAAGTGCCACCT

296/345

FIG. 85A

GACGTCGCGGCCCTCTAGGCCTCCAAAAAAGCCTCCTCACTACTTCT AAAATTAGTCAGCCATGCATGGGGCGAAATGGGCGGAACTGGGCG GAGTTAGGGGGGGATGGGCGGAGTTAGGGGGGGGACTATGGTTGCT GACTAATTGAGATGCATGCTTTGCATACTTCTGCCTGCTGGGGAGCCT ATACTTCTGCCTGCTGGGGAGCCTGGGGACTTTCCACACCCTAACTGA CACACATTCCACAGAATTAATTCCCCTAGTTATTAATAGTAATCAATT ACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA CTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCC ATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGA CTTTCCATTGACGTCAATGGGTGGACTATTTACGGTAAACTGCCCACT TGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACG TCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCT TATGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTA TTACCATGGTGATGCGGTTTTGGCAGTACATCAATGGGCGTGGATACC GGTTTGACTCACGCGGATTTCCAAGTCTCCACCCCATTGACGTCAATG GGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTA ACAACTCCGCCCATTGACGCAAATGGGCGTAGGCGTGTACGGTGG GAGGTCTATATAAGCAGAGCTGGGTACGTGAACCGTCAGATCGCCTG GAGACGCCATCACAGATCTCTCACTATGGATTTTCAGGTGCAGATTAT CAGCTTCCTGCTAATCAGTGCTTCAGTCATAATGTCCAGAGGACAAAT TGTTCTCTCCCAGTCTCCAGCAATCCTGTCTGCATCTCCAGGGGAGAA GGTCACAATGACTTGCAGGGCCAGCTCAAGTGTAAGTTACATCCACT GGTTCCAGCAGAAGCCAGGATCCTCCCCCAAACCCTGGATTTATGCCA CATCCAACCTGGCTTCTGGAGTCCCTGTTCGCTTCAGTGGCAGTGGGT CTGGGACTTCTTACTCTCACAATCAGCAGAGTGGAGGCTGAAGATG GAGGGGGACCAAGCTGGAAATCAAACGTACGGTGGCTGCACCATCT GTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCC TCTGTTGTGTGCCTGCTGAATAACTTCTATCCCAGAGAGGCCAAAGTA CAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCCAGGAGAG CCCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTACGCC TGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTT CAACAGGGGAGAGTGTTGAATTCAGATCCGTTAACGGTTACCAACTA CCTAGACTGGATTCGTGACAACATGCGGCCGTGATATCTACGTATGAT CAGCCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCCTC CCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCC

297/345 FIG. 85B

TAATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCT ATTCTGGGGGGTGGGGTGGGGCAGGACAGCAAGGGGGAGGATTGGG AAGACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCTATGGAACCA GCTGGGGCTCGACAGCTATGCCAAGTACGCCCCCTATTGACGTCAATG ACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGG ACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCAT GGTGATGCGGTTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTG ACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGGAGTT TGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACT CCGCCCATTGACGCAAATGGGCGTAGGCGTGTACGGTGGGAGGTC TATATAAGCAGAGCTGGGTACGTCCTCACATTCAGTGATCAGCACTGA ACACAGACCCGTCGACATGGGTTGGAGCCTCATCTTGCTCTTCCTTGT CGCTGTTGCTACGCGTGTCCTGTCCCAGGTACAACTGCAGCAGCCTGG GGCTGAGCTGGAAGCCTGGGGCCTCAGTGAAGATGTCCTGCAAGG CTTCTGGCTACACATTTACCAGTTACAATATGCACTGGGTAAAACAGA CACCTGGTCGGGGCCTGGAATGGATTGGAGCTATTTATCCCGGAAAT GGTGATACTTCCTACAATCAGAAGTTCAAAGGCAAGGCCACATTGAC TGCAGACAAATCCTCCAGCACAGCCTACATGCAGCTCAGCAGCCTGA CATCTGAGGACTCTGCGGTCTATTACTGTGCAAGATCGACTTACTACG GCGGTGACTGGTACTTCAATGTCTGGGGCGCAGGGACCACGGTCACC GTCTCTGCAGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCC TCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGT CAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCG CCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAG GACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGG GCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACC AAGGTGGACAAGAAGCAGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTT CCTCTTCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCC TGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGG TCAAGTTCAACTGGTACGTGGACGCGTGGAGGTGCATAATGCCAAG ACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAG CGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACA AGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACC ATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCT GCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCT GCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAG AGCAATGGGCAGCCGGAGACAACTACAAGACCACGCCTCCCGTGCT GGACTCCGACGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAA GAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATG AGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGG GTAAATGAGGATCCGTTAACGGTTACCAACTACCTAGACTGGATTCGT

298/345 FIG. 85C

GACAACATGCGGCCGTGATATCTACGTATGATCAGCCTCGACTGTGCC ACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGGAA ATTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGG GTGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGC ATGCTGGGGATGCGGTGGGCTCTATGGAACCAGCTGGGGCTCGACAG CGCTGGATCTCCCGATCCCCAGCTTTGCTTCTCAATTTCTTATTTGCAT AATGAGAAAAAAGGAAAATTAATTTTAACACCAATTCAGTAGTTGA TTGAGCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACAGTGTTCTCT GCACAGATAAGGACAAACATTATTCAGAGGGAGTACCCAGAGCTGAG ACTCCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGAAATATGCTT GTCATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGGTAAGGGCC AATCTGCTCACACAGGATAGAGAGGGCAGGAGCCAGGGCAGAGCAT ATAAGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTCTGACATAG TTGTGTTGGGAGCTTGGATAGCTTGGACAGCTCAGGGCTGCGATTTCG CGCCAAACTTGACGCCAATCCTAGCGTGAAGGCTGGTAGGATTTTATC CCCGCTGCCATCATGGTTCGACCATTGAACTGCATCGTCGCCGTGTCC CAAAATATGGGGATTGGCAAGAACGGAGACCTACCCTGGCCTCCGCT CAGGAACGAGTTCAAGTACTTCCAAAGAATGACCACAACCTCTTCAG TGGAAGGTAAACAGAATCTGGTGATTATGGGTAGGAAAACCTGGTTC TCCATTCCTGAGAAGAATCGACCTTTAAAGGACAGAATTAATATAGTT CTCAGTAGAGAACTCAAAGAACCACCACGAGGAGCTCATTTTCTTGC CAAAAGTTTGGATGATGCCTTAAGACTTATTGAACAACCGGAATTGG CAAGTAAAGTAGACATGGTTTGGATAGTCGGAGGCAGTTCTGTTTACC AGGAAGCCATGAATCAACCAGGCCACCTTAGACTCTTTGTGACAAGG ATCATGCAGGAATTTGAAAGTGACACGTTTTTCCCAGAAATTGATTTG GGGAAATATAAACTTCTCCCAGAATACCCAGGCGTCCTCTCTGA GGTCCAGGAGAAAAAGGCATCAAGTATAAGTTTGAAGTCTACGAGA AGAAAGACTAACAGGAAGATGCTTTCAAGTTCTCTGCTCCCCTCCTAA AGCTATGCATTTTTATAAGACCATGGGACTTTTGCTGGCTTTAGATCA GCCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCCTCCC CCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTA ATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTAT TCTGGGGGTGGGGTGGGCAGGACAGCAAGGGGGAGGATTGGGAA GACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCTATGGAACCAGC TGGGGCTCGAGCTACTAGCTTTGCTTCTCAATTTCTTATTTGCATAATG GCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACAGTGTTCTCTGCA CAGATAAGGACAAACATTATTCAGAGGGAGTACCCAGAGCTGAGACT CCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGAAATATGCTTGTC ATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGGTAAGGGCCAAT CTGCTCACACAGGATAGAGAGGGCAGGGCAGGGCAGAGCATATA AGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTCTGACATAGTTG

299/345 FIG. 85D

TGTTGGGAGCTTGGATCGATCCTCTATGGTTGAACAAGATGGATTGCA CGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTATTCGGCTATGACTG GGCACAACAGACAATCGGCTGCTCTGATGCCGCCGTGTTCCGGCTGTC AGCGCAGGGCCCCGGTTCTTTTTGTCAAGACCGACCTGTCCGGTGC CGACGGCGTTCCTTGCGCAGCTGTGCTCGACGTTGTCACTGAAGCGG GAAGGGACTGGCTATTGGGCGAAGTGCCGGGGCAGGATCTCCTG TCATCTCACCTTGCTCCTGCCGAGAAAGTATCCATCATGGCTGATGCA ATGCGGCGGCTGCATACGCTTGATCCGGCTACCTGCCCATTCGACCAC CAAGCGAAACATCGCATCGAGCGAGCACGTACTCGGATGGAAGCCGG TCTTGTCGATCAGGATGATCTGGACGAAGAGCATCAGGGGCTCGCGC CAGCCGAACTGTTCGCCAGGCTCAAGGCGCGCATGCCCGACGGCGAG GATCTCGTCGTGACCCATGGCGATGCCTGCTTGCCGAATATCATGGTG GAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGCCGGCTGGGTGTG GCGGACCGCTATCAGGACATAGCGTTGGCTACCCGTGATATTGCTGA AGAGCTTGGCGGCGAATGGGCTGACCGCTTCCTCGTGCTTTACGGTAT CGCCGCTCCCGATTCGCAGCGCATCGCCTTCTATCGCCTTCTTGACGA GCCCAACCTGCCATCACGAGATTTCGATTCCACCGCCGCCTTCTATGA AAGGTTGGGCTTCGGAATCGTTTTCCGGGACGCCGGCTGGATGATCCT CCAGCGCGGGATCTCATGCTGGAGTTCTTCGCCCACCCCAACTTGTT TATTGCAGCTTATAATGGTTACAAATAAAGCAATAGCATCACAAATTT CACAAATAAAGCATTTTTTCACTGCATTCTAGTTGTGGTTTGTCCAA ACTCATCAATCTATCTTATCATGTCTGGATCGCGGCCGCGATCCCGTC GAGAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGT TATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAGTG TAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTT GCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTCGTGCCAGCTGCA TTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGC GCTCTTCCGCTTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCT GCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCA CAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCA GCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCC ATAGGCTCCGCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGT CAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCC CCCTGGAAGCTCCCTGTGCGCTCTCCTGTTCCGACCCTGCCGCTTAC CGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCA ATGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAA GCTGGGCTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTT ATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATC

240/345

FIG. 53A

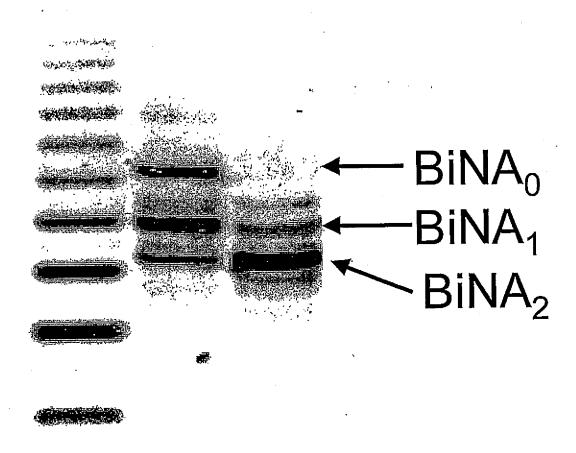
GCGCCTCTTATGTACCCACAAAAATCTATTTCAAAAAAGTTGCTCTA AGAATATAGTTATCAAGTTAAGTAAAATGTCAATAGCCTTTTAATTTA ATTTTTAATTGTTTTATCATTCTTTGCAATAATAAAACATTAACTTTAT ACTTTTTAATTTAATGTATAGAATAGAGATATACATAGGATATGTAAA TAGATACACAGTGTATATGTGATTAAAATATAATGGGAGATTCAATC AATAATGAAAAAATGTGGTGAGAAAAACAGCTGAAAACCCATGTA AAGAGTGTATAAAGAAAGCAAAAAGAGAAGTAGAAAGTAACACAGG GGCATTTGGAAAATGTAAACGAGTATGTTCCCTATTTAAGGCTAGGC ACAAAGCAAGGTCTTCAGAGAACCTGGAGCCTAAGGTTTAGGCTCAC CCATTTCAACCAGTCTAGCAGCATCTGCAACATCTACAATGGCCTTGA CCTTTGCTTTACTGGTGGCCCTCCTGGTGCTCAGCTGCAAGTCAAGCT GCTCTGTGGGCTGTGATCTGCCTCAAACCCACAGCCTGGGTAGCAGG AGGACCTTGATGCTCCTGGCACAGATGAGGAGAATCTCTCTTTTCTCC TGCTTGAAGGACAGACATGACTTTGGATTTCCCCAGGAGGAGTTTGG CAACCAGTTCCAAAAGGCTGAAACCATCCCTGTCCTCCATGAGATGA TCCAGCAGATCTTCAATCTCTTCAGCACAAAGGACTCATCTGCTGCTT GGGATGAGACCCTCCTAGACAAATTCTACACTGAACTCTACCAGCAG CTGAATGACCTGGAAGCCTGTGTGATACAGGGGGTGGGGGTGACAGA GACTCCCTGATGAAGGAGGACTCCATTCTGGCTGTGAGGAAATACT TCCAAAGAATCACTCTCTATCTGAAAGAGAAGAAATACAGCCCTTGT GCCTGGGAGGTTGTCAGAGCAGAAATCATGAGATCTTTTTCTTTGTCA ACAAACTTGCAAGAAAGTTAAGAAGTAAGGAATGAAAACTGGTTCA ACATGGAAATGATTTCATTGATTCGTATGCCAGCTCACCTTTTTATG ATCTGCCATTTCAAAGACTCATGTTTCTGCTATGACCATGACACGATT TAAATCTTTTCAAATGTTTTTAGGAGTATTAATCAACATTGTATTCAG ATCTATTTAAAATATTTTAAAAATATTATTTAATTAACTATTTATAAAAAC AACTTATTTTTGTTCATATTATGTCATGTGCACCTTTGCACAGTGGTTA CATTGAACTTTTGCTATGGAACTTTTTGTACTTGTTTATTCTTTAAAAATG AAATTCCAAGCCTAATTGTGCAACCTGATTACAGAATAACTGGTACA TTTCTGTAAACCAAGTTGTATGTTGTACTCAAGATAACAGGGTGAACC TAACAAATACAATTCTGCTCTCTTGTGTATTTGATTTTGTATGAAAA AAACTAAAAATGGTAATCATACTTAATTATCAGTTATGGTAAATGGT ATGAAGAGAAGAAGGAACG

300/345 FIG. 85E

GCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATG TAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTAC ACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACC TGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAA AAAAGGATCTCAAGAAGATCCTTTGATCTTTCTACGGGGTCTGACGC TCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATC AAAAAGGATCTTCACCTAGATCCTTTTAAAATTAAAAATGAAGTTTTAA ATCAATCTAAAGTATATGAGTAAACTTGGTCTGACAGTTACCAATG CTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCC ATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGG CTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTC ACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCG ATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGC GCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGT TTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTA CATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTC CGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTA TGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCT TTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTA TGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAATACC GCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCT TCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCG ATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCA CCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAA AAGGGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCT TTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGG ATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTTCCGC GCACATTTCCCCGAAAAGTGCCACCT

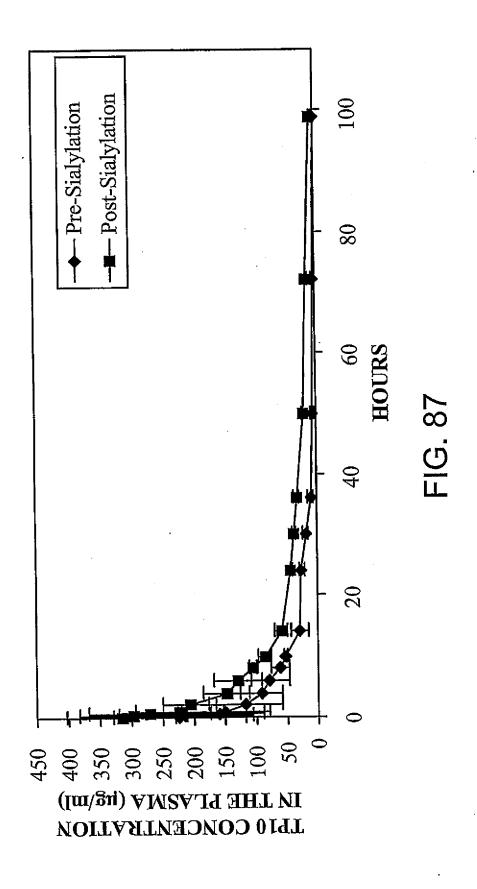
PCT/US02/32263

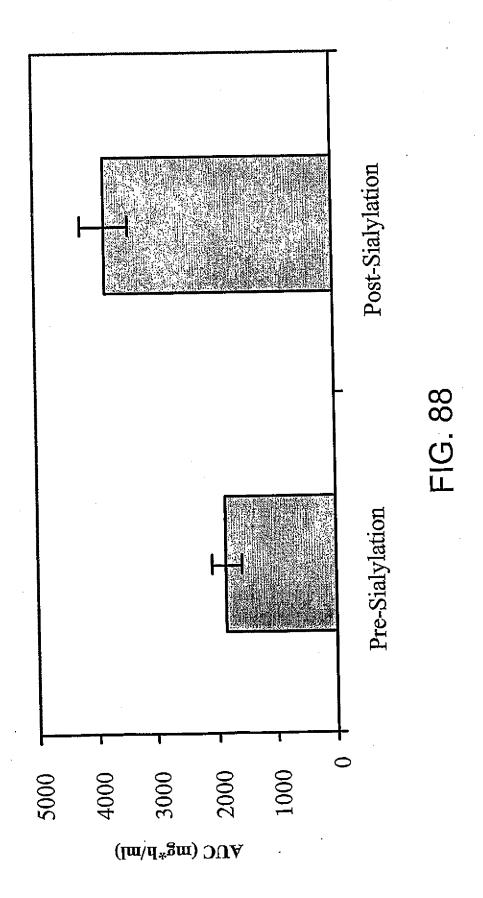
301/345



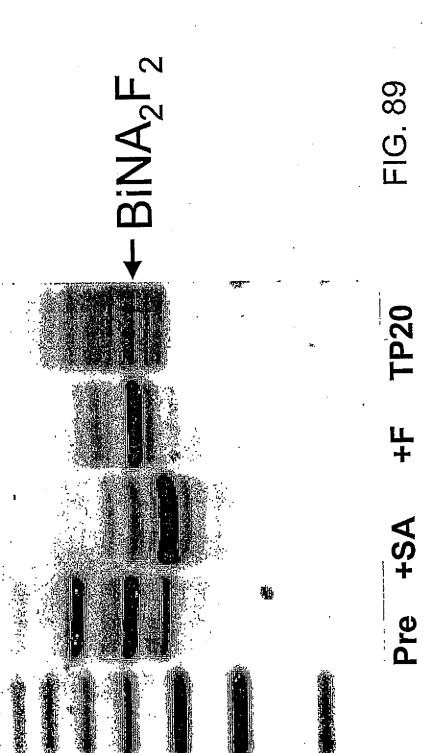
Pre Post

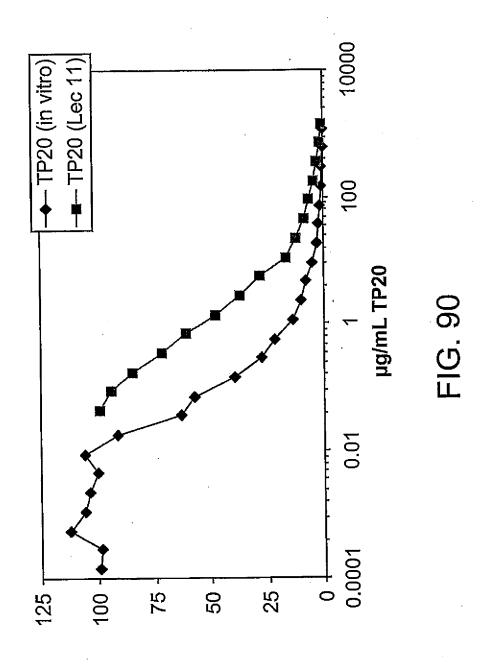
FIG. 86



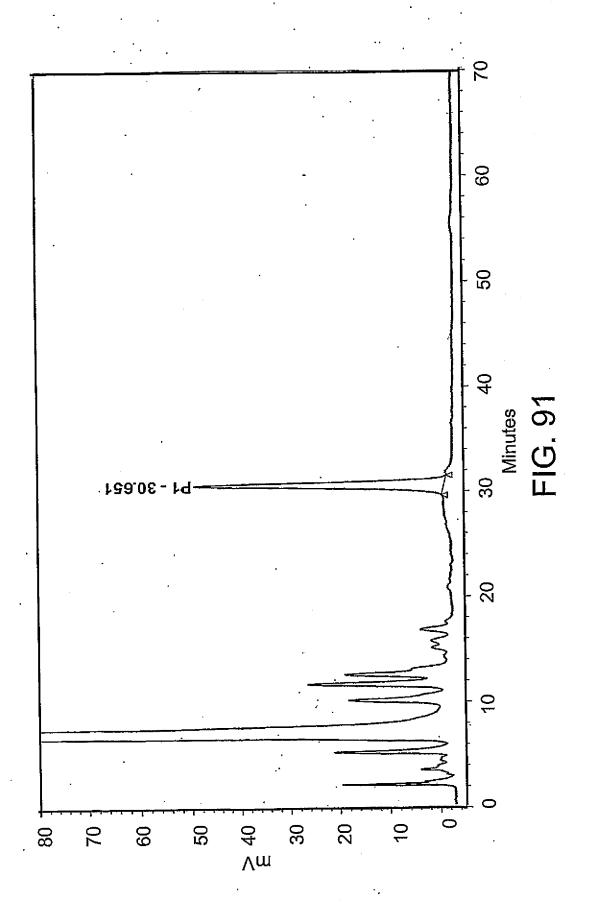


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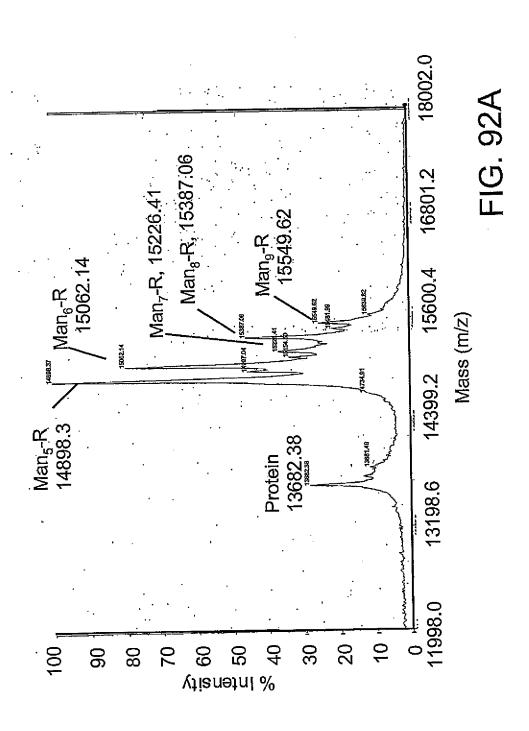


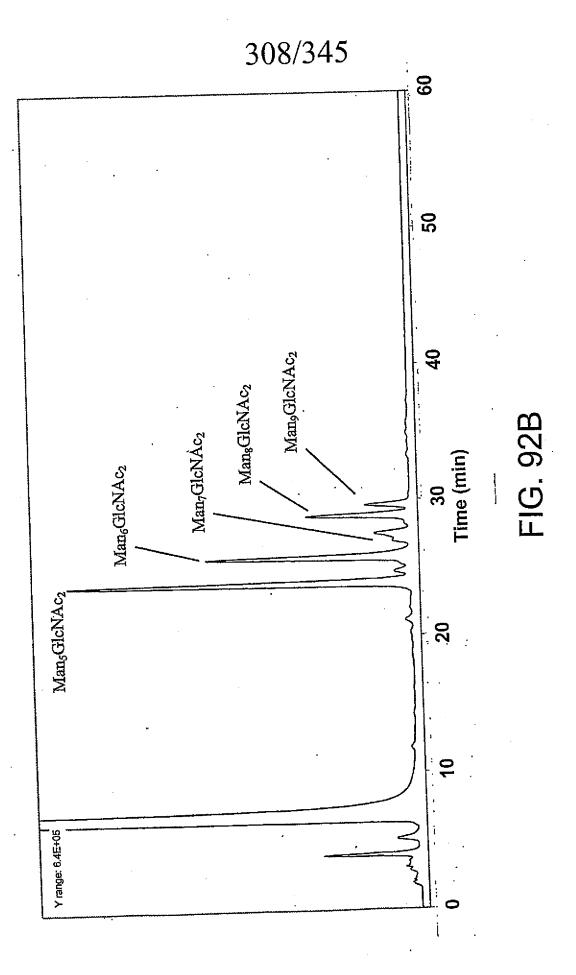


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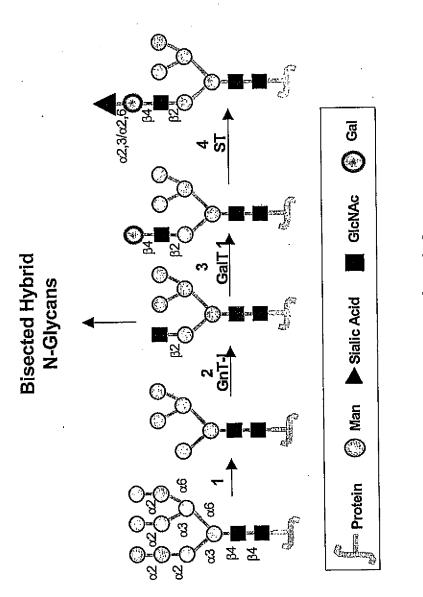
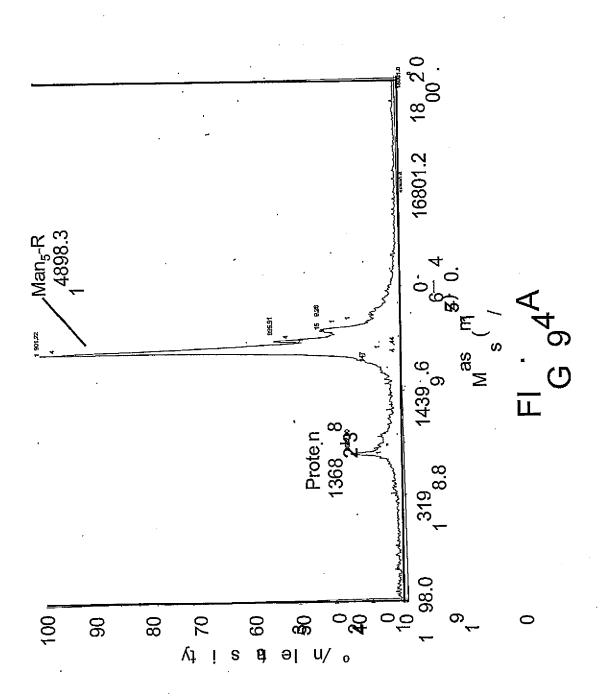
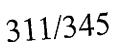
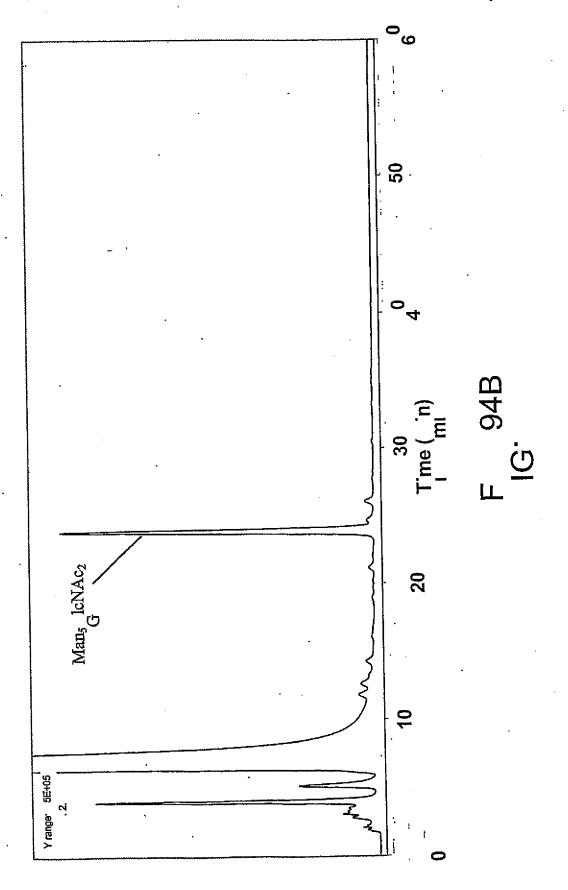
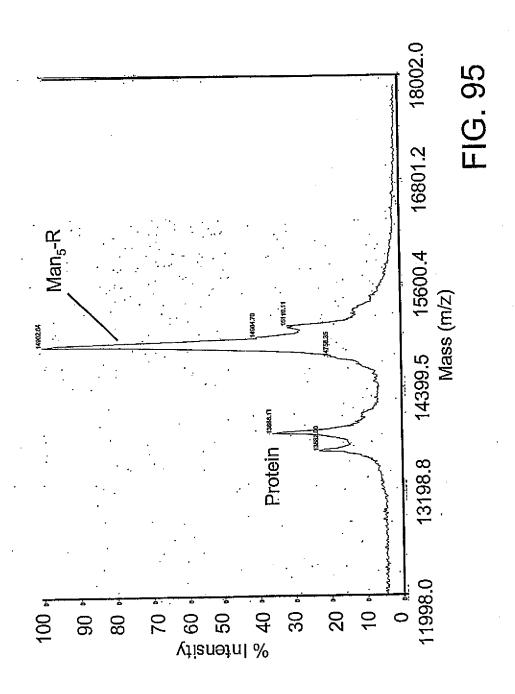


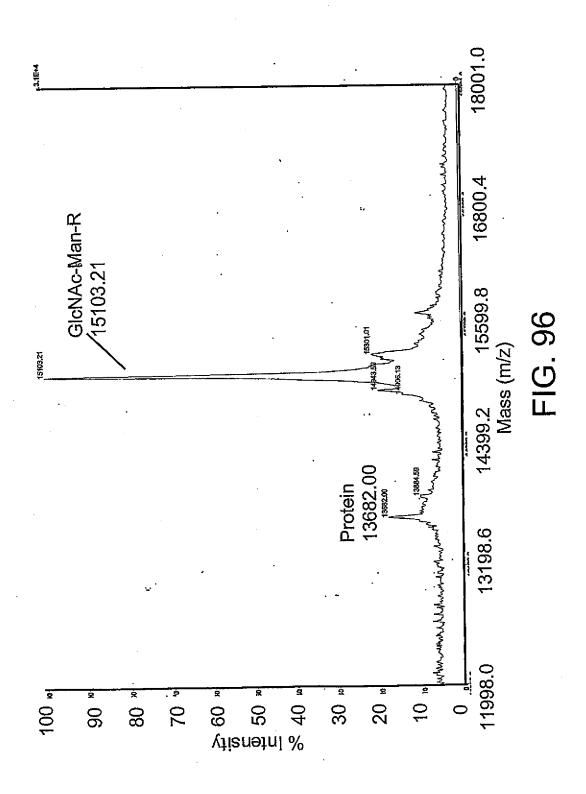
FIG. 93

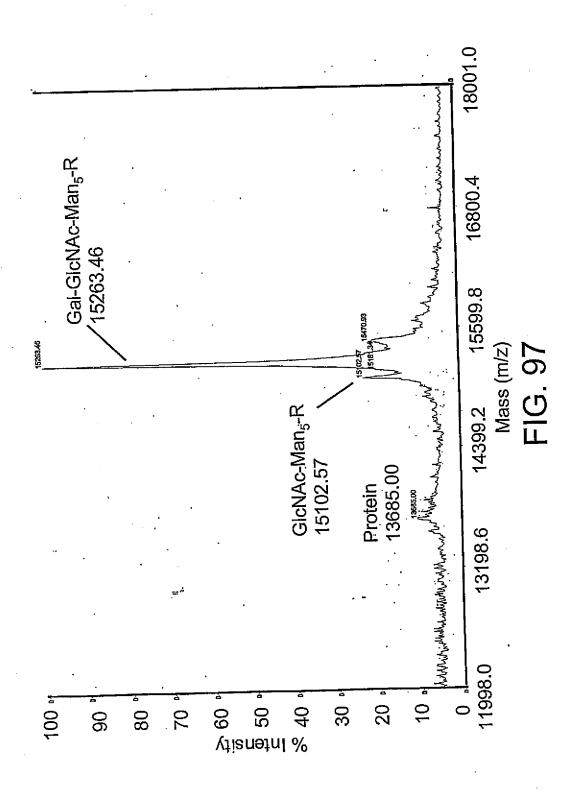


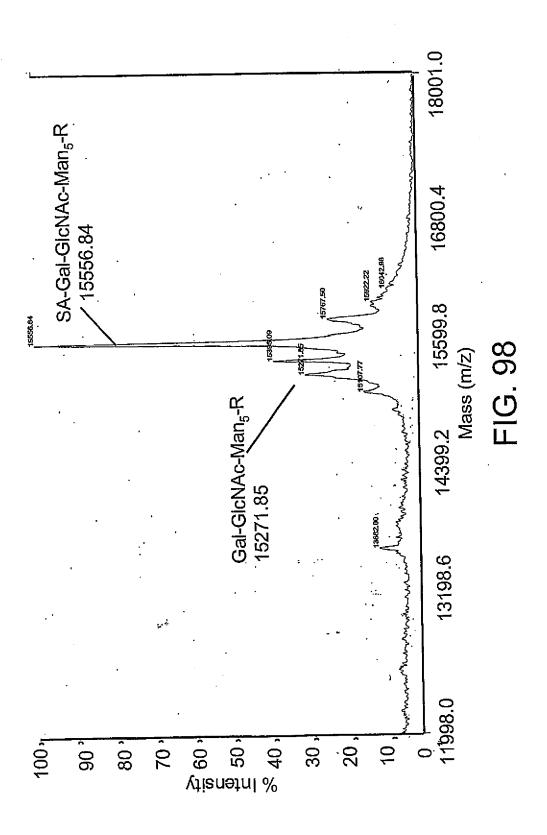












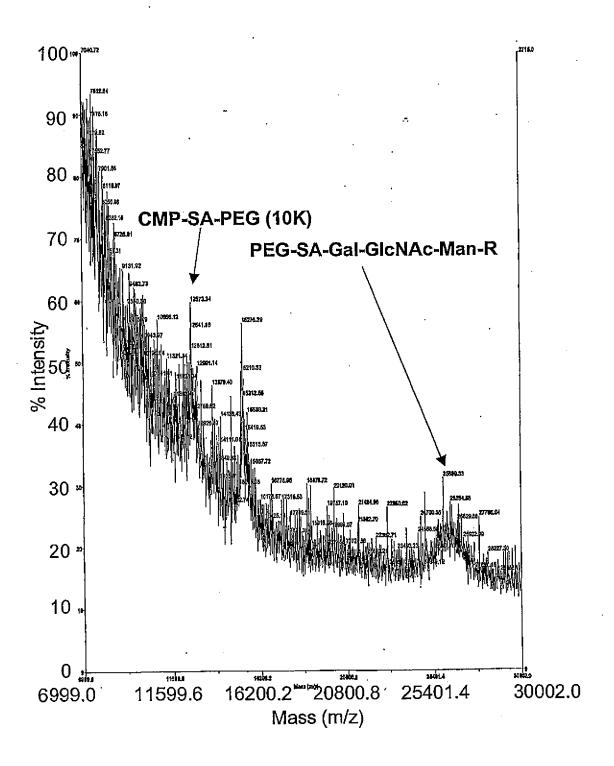


FIG. 99A

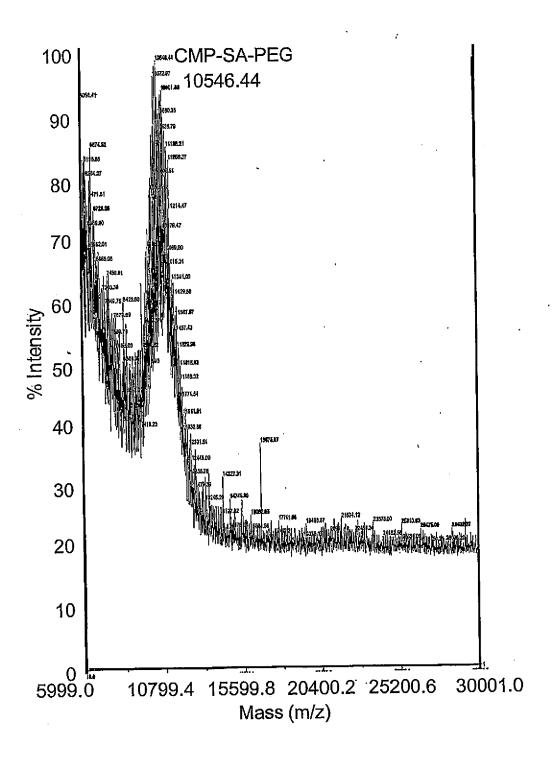
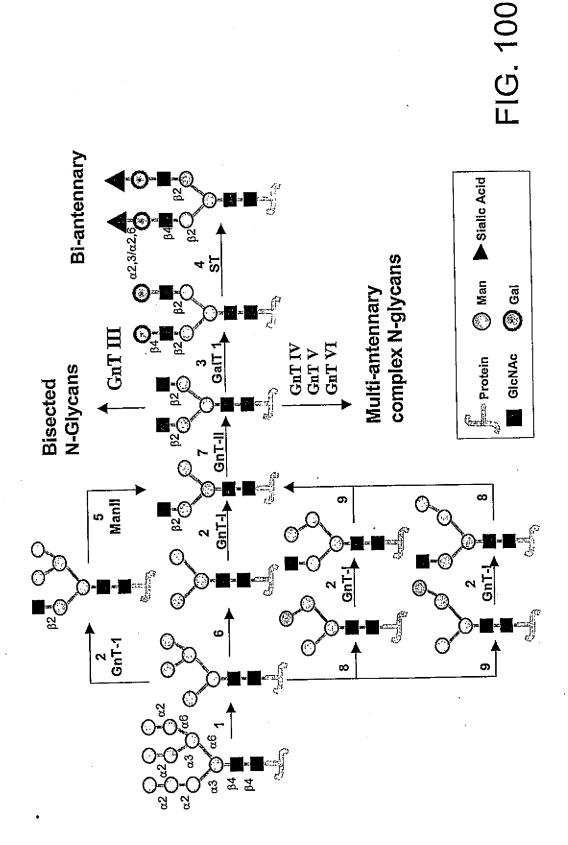
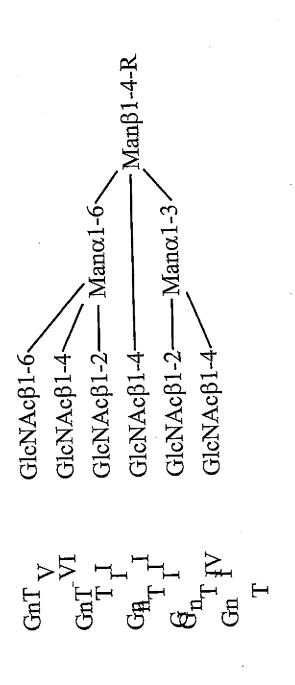
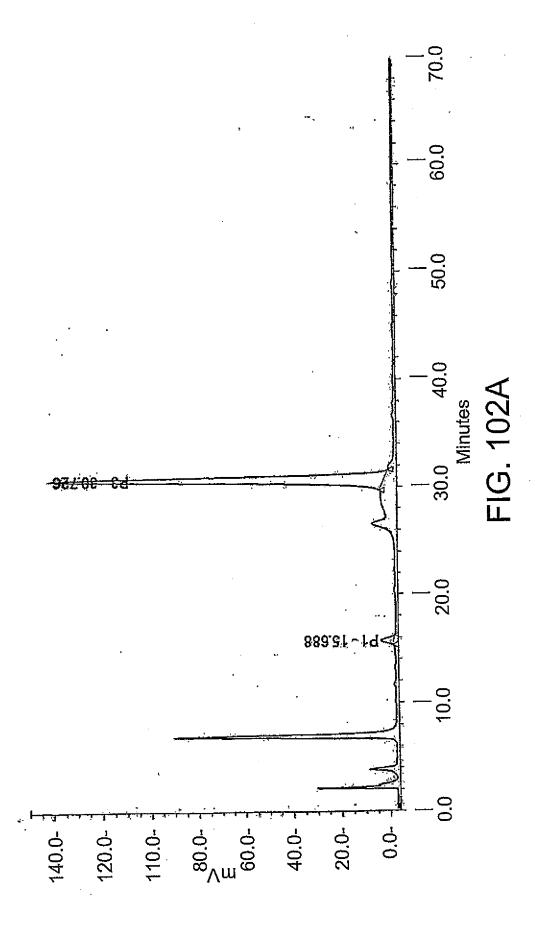


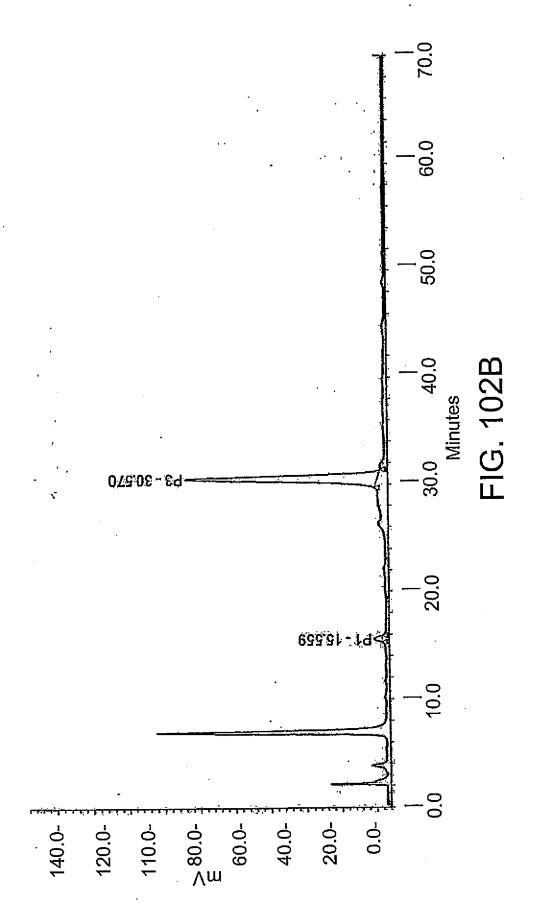
FIG. 99B

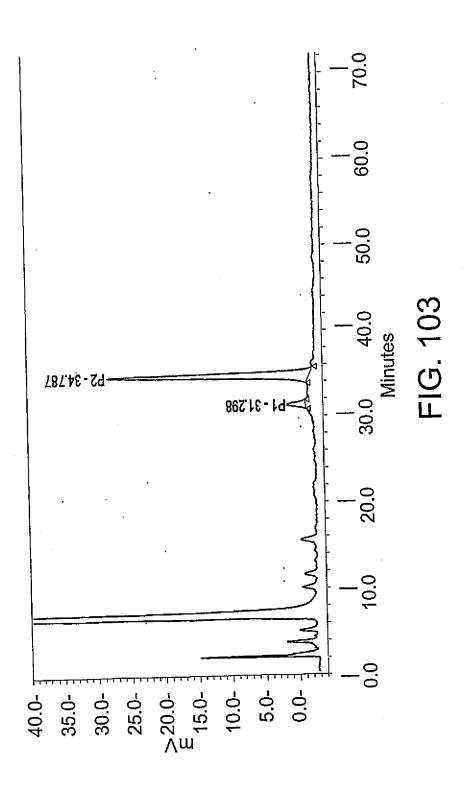


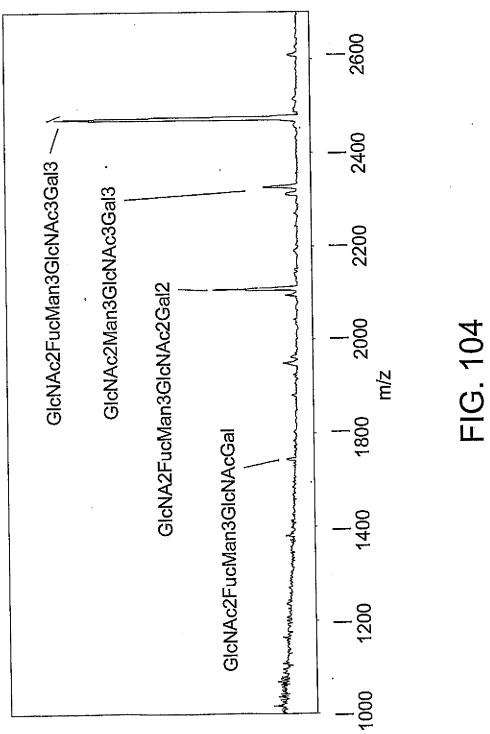


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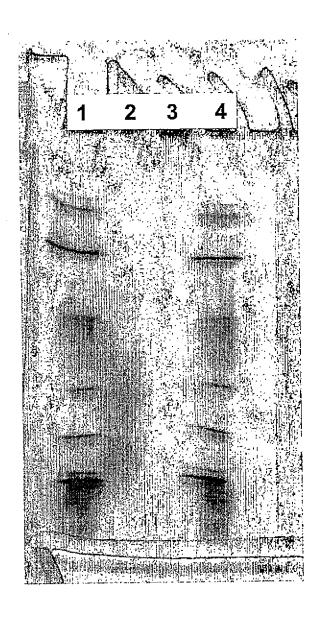


FIG. 105

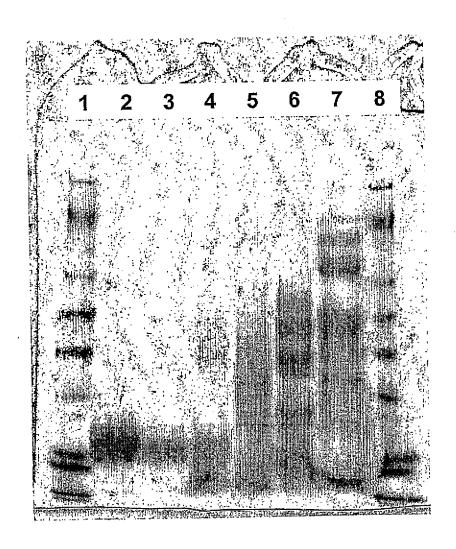


FIG. 106

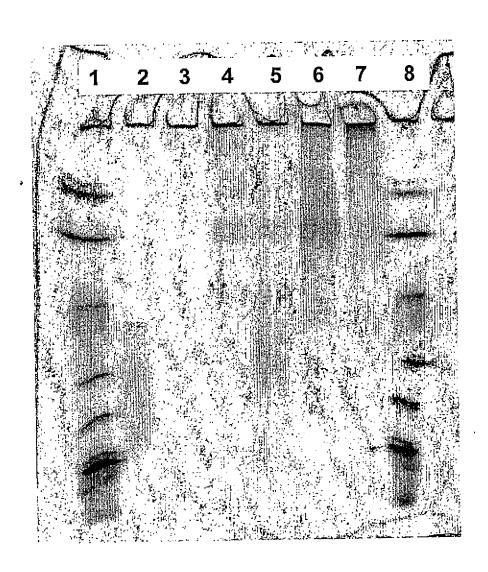


FIG. 107

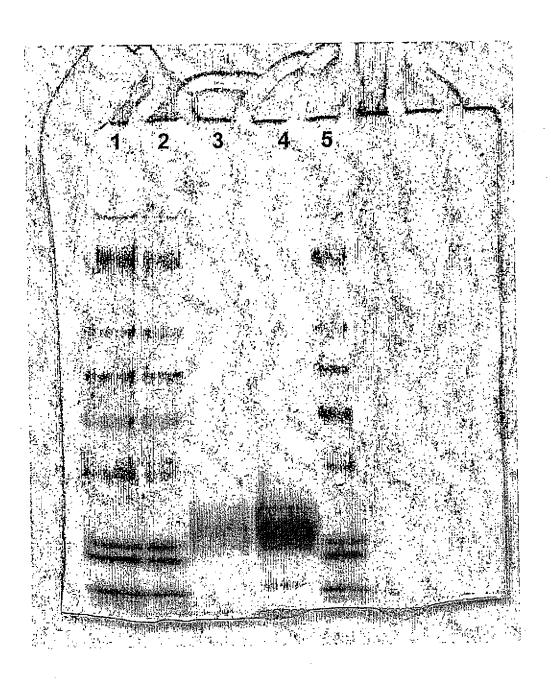


FIG. 108

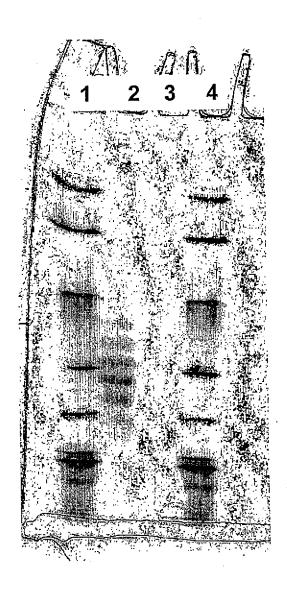


FIG. 109

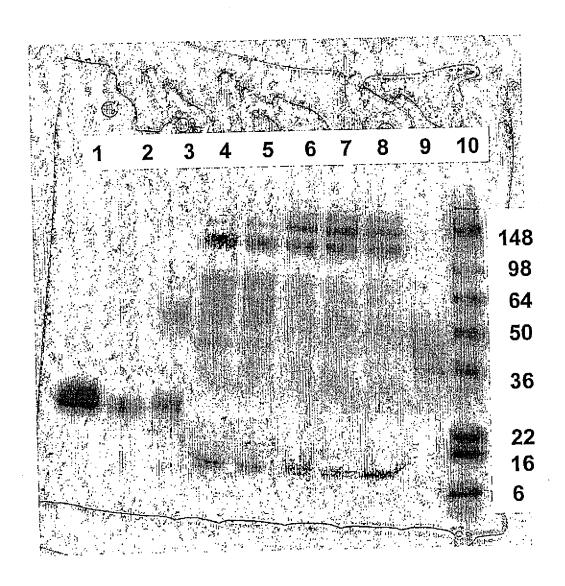


FIG. 110

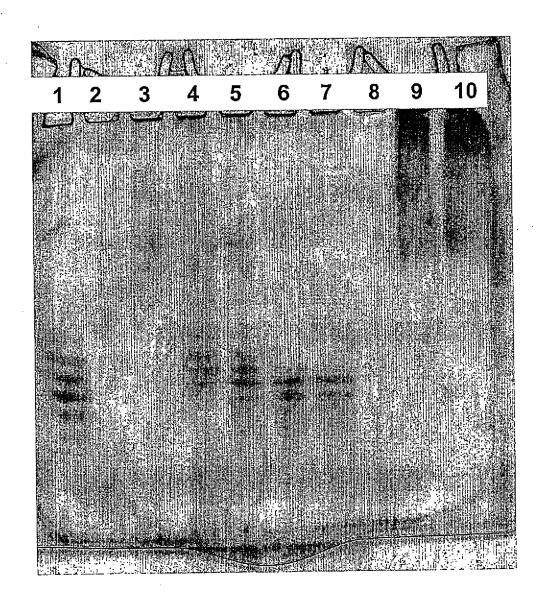
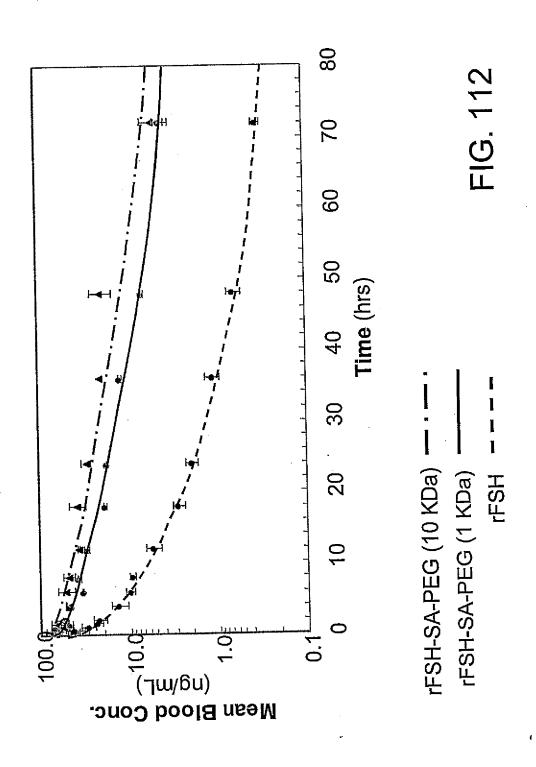
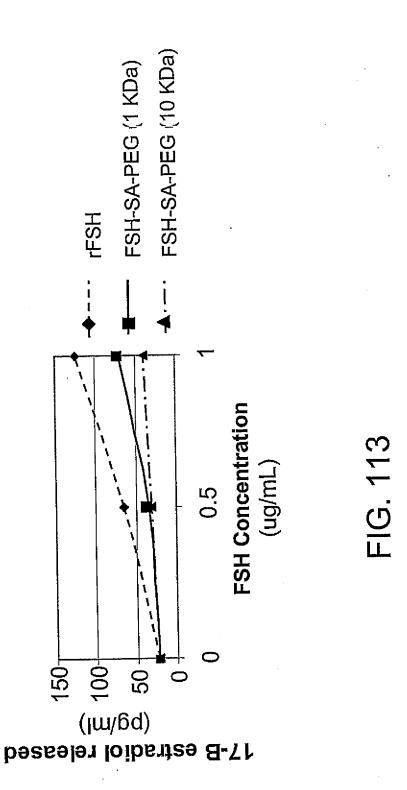


FIG. 111





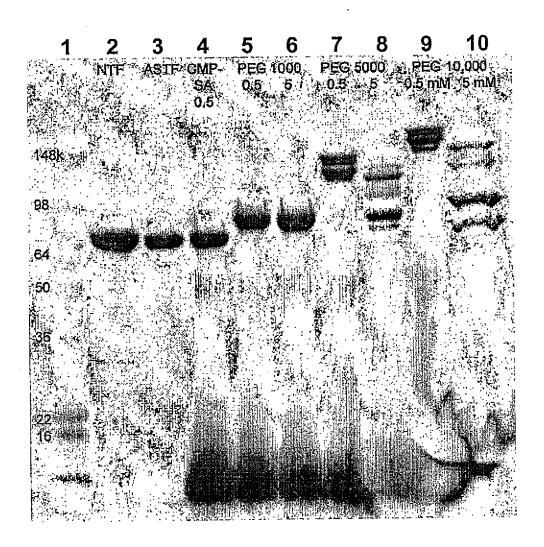


FIG. 114

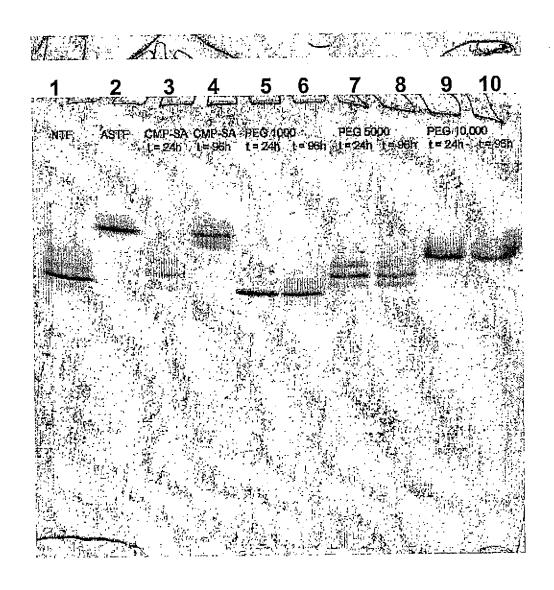


FIG. 115

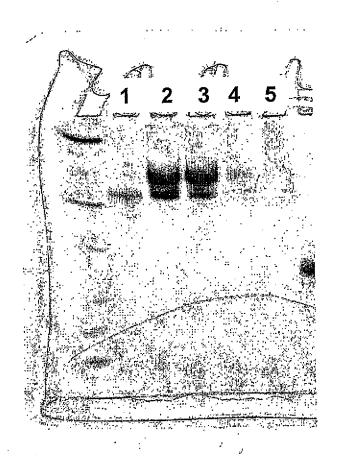
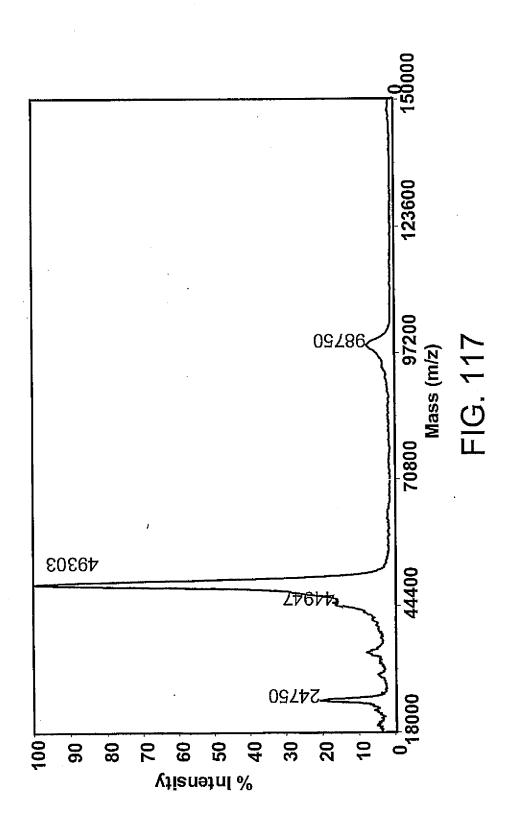
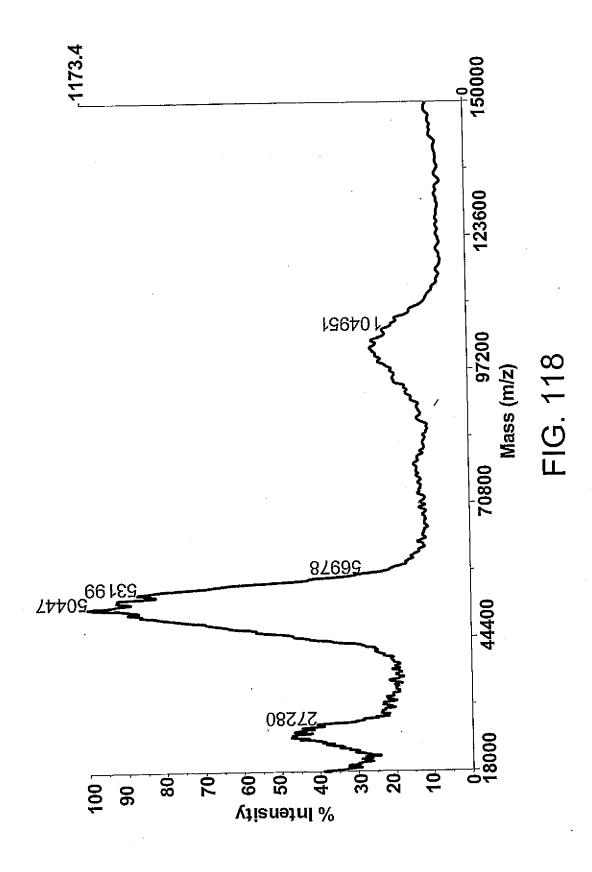
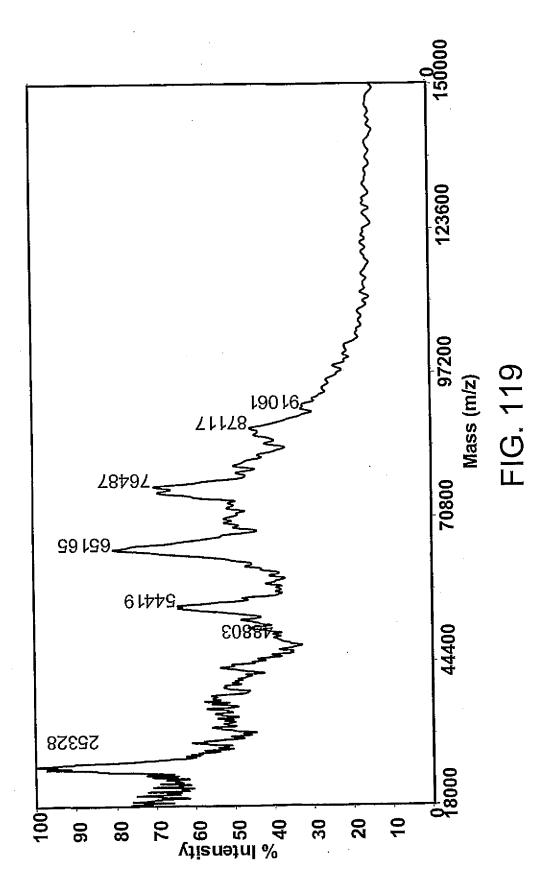


FIG. 116





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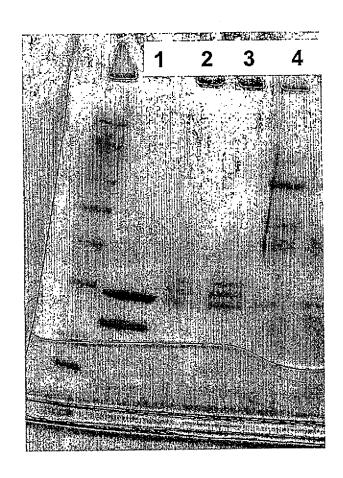


FIG. 120

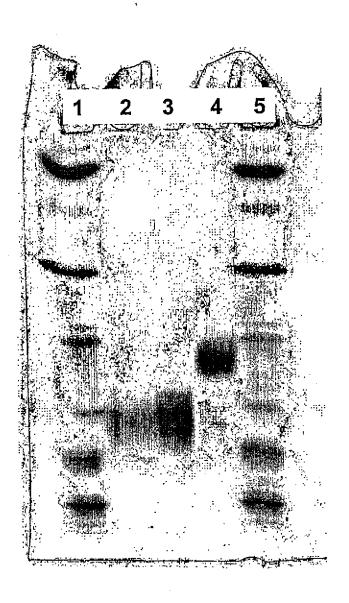


FIG. 121



FIG. 122

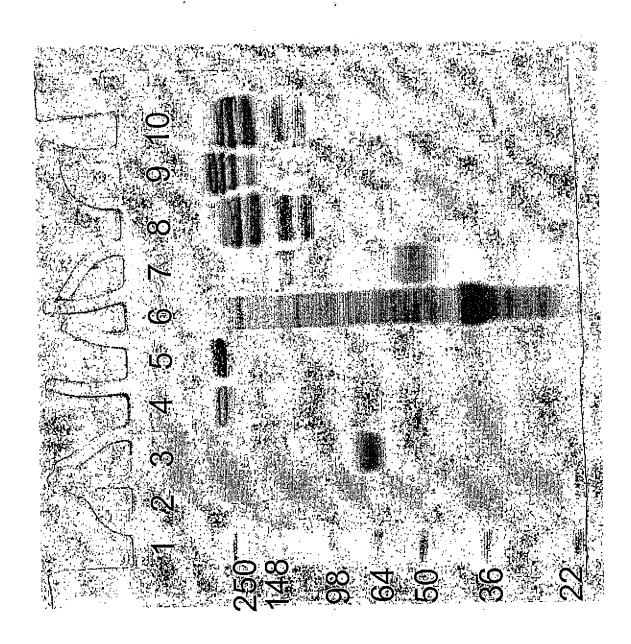


FIG. 123

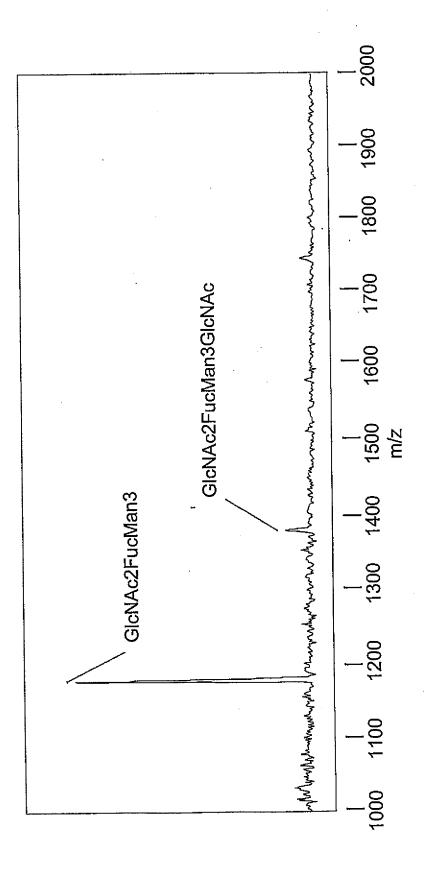


FIG. 124

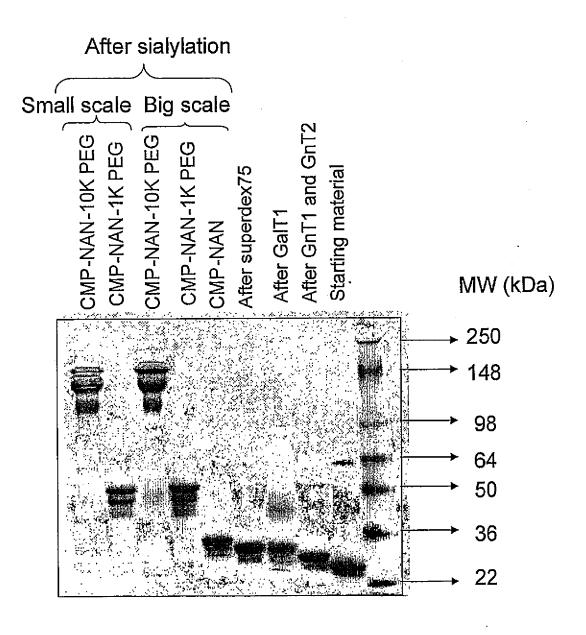


FIG. 125

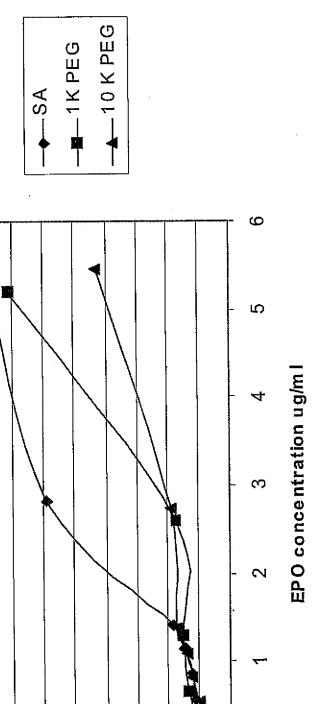


FIG. 126

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3 5

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Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys
50 55 60

Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser 65 70 75 80

Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser 85 90 95

Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp 100 105 110

Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro 115 120 125

Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe 130 135 140

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<212> PRT

<213> Homo sapiens

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Gly Ser Arg Arg Thr Leu Met Leu Leu Ala Gln Met Arg Arg Ile Ser 35 40 45

Leu Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe Pro Gln Glu 50 55 60

Glu Phe Gly Asn Gln Phe Gln Lys Ala Glu Thr Ile Pro Val Leu His 65 70 75 80

Glu Met Ile Gln Gln Ile Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser 85 90 95

Ala Ala Trp Asp Glu Thr Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr 100 105 110

Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Gly Val Gly Val 115 120 125

Thr Glu Thr Pro Leu Met Lys Glu Asp Ser Ile Leu Ala Val Arg Lys 130 135 140

Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro 145 150 155 160

Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser Leu 165 170 175

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<211> 187

<212> PRT

<213> Homo sapiens

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Ser	Ser	Asn 35	Phe	Gln	Сув	Gln	Lуs 40	Leu	Leu	Trp	Gln	Leu 45	Asn	Gly	Arg	
Leu	Glu 50	Tyr	Cys	Leu	Lys	Asp 55	Arg	Met	Asn	Phe	Asp 60	Ile	Pro	Glu	Glu	
Ile 65	Lys	Gln	Leu	Gln	Gln 70	Phe	Gln	Lys	Glu	Asp 75	Ala	Ala	Leu	Thr	Ile 80	
Tyr	Glu	Met	Ъеu	Gln 85	Asn	Ile	Phe	Ala	Ile 90	Phe	Arg	Gln	Asp	Ser 95	Ser	
ser	Thr	Gly	Trp 100	Asn	Glu	Thr	Ile	Val 105	Glu	Asn	Leu	Leu	Ala 110	Asn	Val	
Tyr	His	Gln 115		Asn	His	Leu	Lys 120	Thr	Val	Leu	Glu	Glu 125	Ъуз	Leu	Glu	·
Гуs	Glu 130) Phe	Thr	. Arg	Gly 135	Lys	Leu	. Met	Ser	Ser 140	Leu	ı His	Leu	r F Àa	
Arg 145		туг	Gly	Ar <u>c</u>	; Ile 150	Lev	. His	туг	Leu	. Lys 155	Ala ;	. Ьуа	s Glu	і Туг	ser 160	
His	Суя	: Ala	a Trp	Thr 165	: Ile	· Va]	Arg	y Val	170	ı Ile	e Let	ı Arg	g Ası	1 Phe 175	e Tyr	
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<211> 444

<212> PRT

<213> Homo sapiens

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Leu His Arg Arg Arg Arg Ala Asn Ala Phe Leu Glu Glu Leu Arg Pro

Gly Ser Leu Glu Arg Glu Cys Lys Glu Glu Glu Cys Ser Phe Glu Glu 50 55

Ala Arg Glu Ile Phe Lys Asp Ala Glu Arg Thr Lys Leu Phe Trp Ile 65 70 75 80

Ser Tyr Ser Asp Gly Asp Gln Cys Ala Ser Ser Pro Cys Gln Asn Gly 85 90 95

Gly Ser Cys Lys Asp Gln Leu Gln Ser Tyr Ile Cys Phe Cys Leu Pro 100 105 110

Ala Phe Glu Gly Arg Asn Cys Glu Thr His Lys Asp Asp Gln Leu Ile 115 120 125

Cys Val Asn Glu Asn Gly Gly Cys Glu Gln Tyr Cys Ser Asp His Thr 130 135 140

Gly Thr Lys Arg Ser Cys Arg Cys His Glu Gly Tyr Ser Leu Leu Ala 145 150 155 160

Asp Gly Val Ser Cys Thr Pro Thr Val Glu Tyr Pro Cys Gly Lys Ile 165 170 175

Pro Ile Leu Glu Lys Arg Asn Ala Ser Lys Pro Gln Gly Arg Ile Val 180 185 190

Gly Gly Lys Val Cys Pro Lys Gly Glu Cys Pro Trp Gln Val Leu Leu 195 200 205

Leu Val Asn Gly Ala Gln Leu Cys Gly Gly Thr Leu Ile Asn Thr Ile 210 215 220

Trp Val Val Ser Ala Ala His Cys Phe Asp Lys Ile Lys Asn Trp Arg 225 230 235 240

Asn Leu Ile Ala Val Leu Gly Glu His Asp Leu Ser Glu His Asp Gly 245 250 255

Asp Glu Gln Ser Arg Arg Val Ala Gln Val Ile Ile Pro Ser Thr Tyr 260 265 270

Val	Pro	Gly 275	Thr	Thr	Asn	His	Asp 280	Ile	А1а	ьеи	Leu	285	Ten	TIP	GIII	
Pro	Val 290	Val	Leu	Thr	Asp	His 295	Val	Val	Pro	Leu	Cys	Leu	Pro	Glu	Arg	
Thr 305	Phe	Ser	Glu	Arg	Thr 310	Leu	Ala	Phe	Val	Arg 315	Phe	Ser	Leu	Val	Ser 320	
Gly	Trp	Gly	Gln	Leu 325	Leu	Asp	Arg	Gly	Ala 330	Thr	Ala	Leu	Glu	Leu 335	Met	
Val	Leu	Asn	Val 340	Pro	Arg	Leu	Met	Thr 345	Gln	Asp	Cys	Leu	Gln 350	Gln	Ser	
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Pro	Arg	Pro 435		val	. Lev	ı Leu	Arc 440	, Ala	Pro) Phe	e Pro				-	
		9 1437 DNA Homo	7 o sag	oiens	5											
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Thr Glu Lys Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln 85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile 100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys 115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe 130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly 145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe 165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala 180 185 190

Glu Ala Val Phe Pro Asp Val Asp Tyr Val Asn Pro Thr Glu Ala Glu 195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Gly Thr Gln Ser Phe Asn Asp Phe 210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp 225 230 235 240

Gln Val Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile 245 250 255

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly 260 265 270

Val Lys Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu 275 280 285

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ala Ile Ile Pro His His 290 295 300

Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu 305 310 315

Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys 325 330 335

Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly 340 345 350

Tyr Val Ser Gly Trp Ala Arg Val Phe His Lys Gly Arg Ser Ala Leu 355 360 365

Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu 370 380

Arg Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe 385 390 395 400

His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His 405 410 415

Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp 420 425 430

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Ile Leu Gln Cys Met Gly Cys Cys Phe Ser Arg Ala Tyr Pro Thr Pro 50 55 60

Leu Arg Ser Lys Lys Thr Met Leu Val Gln Lys Asn Val Thr Ser Glu 65 70 75 80

Ser Thr Cys Cys Val Ala Lys Ser Tyr Asn Arg Val Thr Val Met Gly 85 90 95

Gly Phe Lys Val Glu Asn His Thr Ala Cys His Cys Ser Thr Cys Tyr 100 105 110

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Glu Glu Cys Arg Phe Cys Ile Ser Ile Asn Thr Thr Trp Cys Ala Gly
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Tyr Cys Tyr Thr Arg Asp Leu Val Tyr Lys Asp Pro Ala Arg Pro Lys 50 55 60

Ile Gln Lys Thr Cys Thr Phe Lys Glu Leu Val Tyr Glu Thr Val Arg 65 70 75 80

Val Pro Gly Cys Ala His His Ala Asp Ser Leu Tyr Thr Tyr Pro Val 85 90 95

Ala Thr Gln Cys His Cys Gly Lys Cys Asp Ser Asp Ser Thr Asp Cys
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Thr Val Arg Gly Leu Gly Pro Ser Tyr Cys Ser Phe Gly Glu Met Lys 115 120 125

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Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu 35 40 45

Ala Glu Asn Ile Thr Thr Gly Cys Ala Glu His Cys Ser Leu Asn Glu
50 55 60

Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe Tyr Ala Trp Lys Arg
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Met Glu Val Gly Gln Gln Ala Val Glu Val Trp Gln Gly Leu Ala Leu 85 90 95

Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu Leu Val Asn Ser Ser 100 105 110

Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp Lys Ala Val Ser Gly
115 120 125

Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Arg Ala Gln Lys Glu 130 135 140

Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile 145 150 155 160

Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu

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Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg Thr Gly Asp 180 185 190

Arg

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Ser Ala Pro Ala Arg Ser Pro Ser Pro Ser Thr Gln Pro Trp Glu His 20 25 30

Val Asn Ala Ile Gln Glu Ala Arg Arg Leu Leu Asn Leu Ser Arg Asp 35 40 45

Thr Ala Ala Glu Met Asn Glu Thr Val Glu Val Ile Ser Glu Met Phe 50 55 60

Asp Leu Gln Glu Pro Thr Cys Leu Gln Thr Arg Leu Glu Leu Tyr Lys 70 65 Gln Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro Leu Thr Met Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr Pro Glu Thr Ser 105 100 Cys Ala Thr Gln Ile Ile Thr Phe Glu Ser Phe Lys Glu Asn Leu Lys 120 115 Asp Phe Leu Leu Val Ile Pro Phe Asp Cys Trp Glu Pro Val Gln Glu 135 130 <210> 19 <211> 501 <212> DNA <213> Homo sapiens <400> 19 atgaaatata caagttatat cttggctttt cagetetgca tegttttggg ttetettgge 60 tgttactgcc aggacccata tgtaaaagaa gcagaaaacc ttaagaaata ttttaatgca 120 ggtcattcag atgtagcgga taatggaact cttttcttag gcattttgaa gaattggaaa 180 gaggagagtg acagaaaaat aatgcagagc caaattgtct ccttttactt caaacttttt 240 aaaaacttta aagatgacca gagcatccaa aagagtgtgg agaccatcaa ggaagacatg 300 aatgtcaagt ttttcaatag caacaaaaag aaacgagatg acttcgaaaa gctgactaat 360 tatteggtaa etgaettgaa tgtecaaege aaageaatae atgaaeteat eeaagtgatg 420 gctgaactgt cgccagcagc taaaacaggg aagcgaaaaa ggagtcagat gctgtttcga 480 501 ggtcgaagag catcccagta a <210> 20 166 <211> <212> PRT <213> Homo sapiens <400> 20 Met Lys Tyr Thr Ser Tyr Ile Leu Ala Phe Gln Leu Cys Ile Val Leu 10

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Gly Thr Leu Phe Leu Gly Ile Leu Lys Asn Trp Lys Glu Glu Ser Asp 50 55 60

Arg Lys Ile Met Gln Ser Gln Ile Val Ser Phe Tyr Phe Lys Leu Phe 65 70 75 80

Lys Asn Phe Lys Asp Asp Gln Ser Ile Gln Lys Ser Val Glu Thr Ile 85 90 95

Lys Glu Asp Met Asn Val Lys Phe Phe Asn Ser Asn Lys Lys Lys Arg 100 105 110

Asp Asp Phe Glu Lys Leu Thr Asn Tyr Ser Val Thr Asp Leu Asn Val

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Gly Arg Arg Ala Ser Gln 165

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Lys Ile Thr Pro Asn Leu Ala Glu Phe Ala Phe Ser Leu Tyr Arg Gln 50 55 60

Leu Ala His Gln Ser Asn Ser Thr Asn Ile Phe Phe Ser Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu Ser Leu Gly Thr Lys Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu Asn Phe Asn Leu Thr Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe Gln Glu Leu Leu Arg Thr Leu Asn Gln Pro Asp Ser Gln Leu Gln Leu Thr Thr Gly Asn Gly Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp Lys Phe Leu Glu Asp Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr Val Asn Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr Val Glu Lys Gly Thr Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu Asp Arg Asp Thr Val Phe Ala Leu Val Asn Tyr Ile Phe Phe Lys Gly Lys Trp Glu Arg Pro Phe Glu Val Lys Asp Thr Glu Glu Glu Asp Phe His Val Asp Gln Val Thr Thr Val Lys Val Pro Met Met Lys Arg Leu Gly Met Phe Asn Ile Gln His Cys Lys Lys Leu Ser Ser Trp Val Leu Leu Met Lys Tyr Leu Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp Glu Gly Lys Leu Gln His Leu Glu

Asn Glu Leu Thr His Asp Ile Ile Thr Lys Phe Leu Glu Asn Glu Asp 290 Arg Arg Ser Ala Ser Leu His Leu Pro Lys Leu Ser Ile Thr Gly Thr 310 Tyr Asp Leu Lys Ser Val Leu Gly Gln Leu Gly Ile Thr Lys Val Phe 330 325 Ser Asn Gly Ala Asp Leu Ser Gly Val Thr Glu Glu Ala Pro Leu Lys 345 340 Leu Ser Lys Ala Val His Lys Ala Val Leu Thr Ile Asp Glu Lys Gly 360 355 Thr Glu Ala Ala Gly Ala Met Phe Leu Glu Ala Ile Pro Met Ser Ile 375 370 Pro Pro Glu Val Lys Phe Asn Lys Pro Phe Val Phe Leu Met Ile Glu 400 395 385 Gln Asn Thr Lys Ser Pro Leu Phe Met Gly Lys Val Val Asn Pro Thr 410 405 Gln Lys <210> 23 <211> 2004 <212> DNA <213> Homo sapiens <400> 23 gctaacctag tgcctatagc taaggcaggt acctgcatcc ttgtttttgt ttagtggatc 60 ctctatectt cagagactct ggaacccctg tggtcttctc ttcatctaat gaccctgagg 120 ggatggagtt ttcaagtcct tccagagagg aatgtcccaa gcctttgagt agggtaagca 180 tcatggctgg cagcctcaca ggtttgcttc tacttcaggc agtgtcgtgg gcatcaggtg 240 cccgccctg catccctaaa agcttcggct acagctcggt ggtgtgtgtc tgcaatgcca 300 catactgtga ctcctttgac cccccgacct ttcctgccct tggtaccttc agccgctatg 360 agagtacacg cagtgggcga cggatggagc tgagtatggg gcccatccag gctaatcaca 420

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Pro Met Ala Ser Cys Asp Phe Ser Ile Arg Thr Tyr Thr Tyr Ala Asp 165 170 175

Thr Pro Asp Asp Phe Gln Leu His Asn Phe Ser Leu Pro Glu Glu Asp 180 185 190

Thr Lys Leu Lys Ile Pro Leu Ile His Arg Ala Leu Gln Leu Ala Gln

Arg Pro Val Ser Leu Leu Ala Ser Pro Trp Thr Ser Pro Thr Trp Leu

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Lys Thr Asn Gly Ala Val Asn Gly Lys Gly Ser Leu Lys Gly Gln Pro 225 230 235 240

Gly Asp Ile Tyr His Gln Thr Trp Ala Arg Tyr Phe Val Lys Phe Leu 245 250 255

Asp Ala Tyr Ala Glu His Lys Leu Gln Phe Trp Ala Val Thr Ala Glu 260 265 270

Asn Glu Pro Ser Ala Gly Leu Leu Ser Gly Tyr Pro Phe Gln Cys Leu 275 280 285

Gly Phe Thr Pro Glu His Gln Arg Asp Phe Ile Ala Arg Asp Leu Gly 290 295 300

Pro Thr Leu Ala Asn Ser Thr His His Asn Val Arg Leu Leu Met Leu 305 310 315

Asp Asp Gln Arg Leu Leu Leu Pro His Trp Ala Lys Val Val Leu Thr 325 330 335

Asp Pro Glu Ala Ala Lys Tyr Val His Gly Ile Ala Val His Trp Tyr 340 345 350

Leu Asp Phe Leu Ala Pro Ala Lys Ala Thr Leu Gly Glu Thr His Arg 355 360 365

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Val Arg Asn Phe Val Asp Ser Pro Ile Ile Val Asp Ile Thr Lys Asp 435 440 445

Thr Phe Tyr Lys Gln Pro Met Phe Tyr His Leu Gly His Phe Ser Lys 450 455 460

Phe Ile Pro Glu Gly Ser Gln Arg Val Gly Leu Val Ala Ser Gln Lys 465 470 475 480

Asn Asp Leu Asp Ala Val Ala Leu Met His Pro Asp Gly Ser Ala Val
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Val Val Val Leu Asn Arg Ser Ser Lys Asp Val Pro Leu Thr Ile Lys 500 505 510

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Arg Val Glu Tyr Cys Trp Cys Asn Ser Gly Arg Ala Gln Cys His Ser 65 70 75 80

- Val Pro Val Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn Gly Gly Thr 85 90 95
- Cys Gln Gln Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro Glu 100 105 110
- Gly Phe Ala Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr 115 120 125
- Glu Asp Gln Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala Glu Ser 130 135 140
- Gly Ala Glu Cys Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro 145 150 155 160
- Tyr Ser Gly Arg Pro Asp Ala Ile Arg Leu Gly Leu Gly Asn His 165 170 175
- Asn Tyr Cys Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys Tyr Val
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- Ser Glu Gly Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg 210 215 220
- Gly Thr His Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn 225 230 235
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- Gln Ala Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly 260 265 270
- Asp Ala Lys Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp 275 280 285
- Glu Tyr Cys Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr

290 295 300

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Ser His Pro Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro 325 330 335

Gly Glu Arg Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile 340 345 350

Leu Ser Ala Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu 355 360 365

Thr Val Ile Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu 370 375 380

Gln Lys Phe Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp 385 390 395

Asp Thr Tyr Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser 405 410 415

Ser Arg Cys Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro 420 425 430

Pro Ala Asp Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly 435 440 445

Tyr Gly Lys His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys 450 455 460

Glu Ala His Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His 465 470 475 480

Leu Leu Asn Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr 485 490 495

Arg Ser Gly Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp 500 505 510

Ser Gly Gly Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val 515 520 525

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Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val 50 55 60

Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile 65 70 75 80

Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln 85 90 95

Ala Glu Val Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser 100 105 110

- His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser 115 120 125
- Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp 130 135 140
- Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu 145 150 155 160
- Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser 165 170 175
- Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile 180 185 190
- Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr 195 200 205
- Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly 210 215 220
- Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp 225 230 235 240
- Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr 245 250 255
- Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val 260 265 270
- Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile 275 280 285
- Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser 290 295 300
- Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met 305 310 315 320

Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His 325 330 335

- Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro 340 345 350
- Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp 355 360 365
- Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser 370 380
- Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr 385 390 395 400
- Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro 405 410 415
- Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn 420 425 430
- Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met 435 440 445
- Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu 450 455 460
- Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu 465 470 475 480
- Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro 485 490 495
- His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys 500 505
- Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe 515 520 525
- Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp 530 535 540
- Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg

545 550 555 560

Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu 565 570 575

Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val 580 585

Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu 595 600 605

Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp 610 615 620

Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val 625 630 635 640

Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp 645 650 655

Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe 660 665 670

Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr 675 680 685

Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro 690 695 700

Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly 705 710 715 720

Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp 725 730 735

Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys
740 745 750

Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Ser Arg His Arg 755 760 765

Ser Thr Arg Gln Lys Gln Phe Asn Ala Thr Thr Ile Pro Glu Asn Asp 770 775 780

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Ile	Gln	Asn	Val	Ser 805	Ser	Ser	Asp	Leu	Leu 810	Met	Leu	Leu	Arg	Gln 815	Ser
Pro	Thr	Pro	His 820	Gly	Leu	Ser	Leu	Ser 825	Asp	Leu	Gln	Glu	Ala 830	Lys	Tyr
Glu	Thr	Phe 835	Ser	Asp	Asp	Pro	Ser 840	Pro	Gly	Ala	Ile	Asp 845	Ser	Asn	Asn
Ser	Leu 850	Ser	Glu	Met	Thr	His 855	Phe	Arg	Pro	Gln	Leu 860	His	His	Ser	Gly
Asp 865	Met	Val	Phe	Thr	Pro 870	Glu	Ser	Gly	Leu	Gln 875	Leu	Arg	Leu	Asn	Glu 880
Гув	Leu	Gly	Thr	Thr 885	Ala	Ala	Thr	Glu	Leu 890	Lys	Гуs	Leu	Asp	Phe 895	Lys
Val	Ser	Ser	Thr 900	Ser	Asn	Asn	Leu	Ile 905	Ser	Thr	Ile	Pro	Ser 910	Asp	Asn
Leu	Ala	Ala 915	Gly	Thr	Asp	'Asn	Thr 920		Ser	Leu	Gly	Pro 925	Pro	Ser	Met
Pro	Val 930		Туr	Asp	Ser	Gln 935	Leu	qaA .	Thr	Thr	Ьеи 940	Phe	Gly	Lys	Lys
Ser 945		Pro	Leu	Thr	Glu 950		Gly	Gly	Pro	955	. Ser	Leu	. Ser	Glu	Glu 960
Asn	Asn	. Asp	Ser	Ьув 965		Leu	. Glu	ı Ser	- Gly 970	r Leu	. Met	Asn	Ser	Gln 975	Glu
ser	· Ser	Trp	Gly 980		Asn	. Val	. Ser	985		Glu	. Ser	Gly	990	Leu	. Phe
Lys	Gly	Lys 995		, Ala	. His	: Gly	Pro 100		a Le	eu Le	eu Th	r Ly 1(/s A	sp A	Asn Ala

Leu	Phe 1010	Lys	Val.	Ser	Ile	Ser 1015	Leu	Leu	Lys	Thr	Asn 1020	Lys	Thr	Ser
Asn	Asn 1025	Ser	Ala	Thr	Asn	Arg 1030	ГÀЗ	Thr	His	Ile	Asp 1035	Gly	Pro	Ser
Leu	Leu 1040		Glu	Asn	Ser	Pro 1045	Ser	Val	Trp	Gln	Asn 1050	Ile	Leu	Glu
Ser	Asp 1055		Glu	Phe	Lys	Ьув 1060	Val	Thr	Pro	Leu	Ile 1065	His	Asp	Arg
Met	Leu 1070	Met	Asp	Lys	Asn	Ala 1075	Thr	Ala	Leu	Arg	Leu 1080	.Asn	His	Met
Ser	Asn 1085		Thr	Thr	Ser	Ser 1090	Ьуs	Asn	Met	Glu	Met 1095	Val	Gln	Gln
Lys	Lys 1100		Gly	Pro	Ile	Pro 1105		Asp	Ala	Gln	Asn 1110	Pro	Asp	Met
Ser	Phe 1115		Lys	Met	Leu	Phe 1120	Leu	Pro	Glu	Ser	Ala 1125	Arg	Trp	Ile
Gln	Arg 1130		His	Gly	Lys	Asn 1135	Ser ·	Leu	Asn	. Ser	Gly 1140	Gln	Gly	Pro
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Gly	Gln 1160		Phe	Leu	Ser	Glu 1165	Lys	Asn	. Lys	val	. Val 1170	Val	. Gly	, Lys
Gly	Glu 1175		Thr	· Lys	Asp	Val 1180		Leu	ι Ъуз	s Glu	Met 118	Va]	. Phe	e Pro
Ser	Ser 1190		ı Asn	Leu	Phe	Leu 1195		: Asr	ı Leı	ı Asp	Asn 120	Lei O	ı His	s Glu
Asr	1 Asn 1205		His	. Asr	ı Glr	ı Glu 1210		з Гуз	; Ile	e Glr	ı Glu 121	Glı 5	ı Ile	e Glu

Lys Lys Glu Thr Leu Ile Gln Glu Asn Val Val Leu Pro Gln Ile His Thr Val Thr Gly Thr Lys Asn Phe Met Lys Asn Leu Phe Leu Leu Ser Thr Arg Gln Asn Val Glu Gly Ser Tyr Asp Gly Ala Tyr Ala Pro Val Leu Gln Asp Phe Arg Ser Leu Asn Asp Ser Thr Asn Arg Thr Lys Lys His Thr Ala His Phe Ser Lys Lys Gly Glu Glu Glu Asn Leu Glu Gly Leu Gly Asn Gln Thr Lys Gln Ile Val Glu Lys Tyr Ala Cys Thr Thr Arg Ile Ser Pro Asn Thr Ser Gln Gln Asn Phe Val Thr Gln Arg Ser Lys Arg Ala Leu Lys Gln Phe Arg Leu Pro Leu Glu Glu Thr Glu Leu Glu Lys Arg Ile Ile Val Asp Asp Thr Ser Thr Gln Trp Ser Lys Asn Met Lys His Leu Thr Pro . 1365 Ser Thr Leu Thr Gln Ile Asp Tyr Asn Glu Lys Glu Lys Gly Ala Ile Thr Gln Ser Pro Leu Ser Asp Cys Leu Thr Arg Ser His Ser Ile Pro Gln Ala Asn Arg Ser Pro Leu Pro Ile Ala Lys Val Ser Ser Phe Pro Ser Ile Arg Pro Ile Tyr Leu Thr Arg Val Leu Phe Gln Asp Asn Ser Ser His Leu Pro Ala Ala Ser Tyr Arg Lys 1430 1435 1440

Asp Ser Gly Val Gln Glu Ser Ser His Phe Leu Gln Gly Ala Lys 1445 1450 1455

Lys Asn Asn Leu Ser Leu Ala Ile Leu Thr Leu Glu Met Thr Gly 1460 1465 1470

Asp Gln Arg Glu Val Gly Ser Leu Gly Thr Ser Ala Thr Asn Ser 1475 1480 1485

Val Thr Tyr Lys Lys Val Glu Asn Thr Val Leu Pro Lys Pro Asp 1490 1495 1500

Leu Pro Lys Thr Ser Gly Lys Val Glu Leu Leu Pro Lys Val His 1505 1510 1515

Ile Tyr Gln Lys Asp Leu Phe Pro Thr Glu Thr Ser Asn Gly Ser 1520 1525 1530

Pro Gly His Leu Asp Leu Val Glu Gly Ser Leu Leu Gln Gly Thr 1535 1540 1545

Glu Gly Ala Ile Lys Trp Asn Glu Ala Asn Arg Pro Gly Lys Val 1550 1560

Pro Phe Leu Arg Val Ala Thr Glu Ser Ser Ala Lys Thr Pro Ser 1565 1570 1575

Lys Leu Leu Asp Pro Leu Ala Trp Asp Asn His Tyr Gly Thr Gln 1580 1585 1590

Ile Pro Lys Glu Glu Trp Lys Ser Gln Glu Lys Ser Pro Glu Lys 1595 1600 1605

Thr Ala Phe Lys Lys Lys Asp Thr Ile Leu Ser Leu Asn Ala Cys 1610 1620

Glu Ser Asn His Ala Ile Ala Ala Ile Asn Glu Gly Gln Asn Lys 1625 1630 1635

Pro Glu Ile Glu Val Thr Trp Ala Lys Gln Gly Arg Thr Glu Arg 1640 1645 1650

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Asp	Asp 1685		Ile	ser		Glu 1690	Met	ГÀв	Lys	Glu	Asp 1695	Phe	Asp	Ile
Tyr	Asp 1700		Asp	Glu	Asn	Gln 1705	Ser	Pro	Arg	Ser	Phe 1710	Gln	ГÀЗ	Ьуз
Thr	Arg 1715		Tyr	Phe	Ile	Ala 1720	Ala	Val	Glu	Arg	Leu 1725	Trp	Asp	Tyr
Gly	Met 1730		Ser	Ser	Pro	His 1735	Val	Leu	Arg	Asn	Arg 1740	Ala	Gln	Ser
Gly	Ser 1745		Pro	Gln	Р'nе	Lys 1750	Lys	Val	Val	Phe	Gln 1755	Glu	Phe	Thr
Asp	Gly 1760		Phe	Thr	Gln	Pro 1765	Leu	Tyr	Arg	Gly	Glu 1770	Leu	Asn	Glu
His	Leu 1775		Leu	Leu	Gly	Pro 1780	Tyr	Ile	Arg	Ala	Glu 1785	Val	Glu	Asp
Asn	Ile 1790		Val	Thr	Phe	Arg 1795		Gln	Ala	. Ser	Arg 1800	Pro	Tyr	Ser
Phe	Туг 1805		Ser	Leu	Ile	Ser 1810		Glu	Glu	Asp	Gln 1815	Arg	Gln	Gl3
Ala	Glu 1820		Arg	Lys	Àsn	Phe 1825	Val	Lys	Pro	Asr	1830	Thr	. Lys	Thi
Tyr	Phe 1835		Lys	val	. Glr	1840		Met	: Ala	Pro	Thr 1845	Lys ;	. As <u>r</u>	Glı
Phe	Asp 1850		ь Гр	a Ala	ı Tr <u>r</u>	Ala 1855	Tyr	: Phe	e Sei	. Asp	Val 1860	Asp)	Let	ı Gl

Lys	Asp 1865	Val	His	Ser	Gly	Leu 1870		Gly	Pro	Leu	Leu 1875	Val	Cys	His
Thr	Asn 1880	Thr	Leu	Asn	Pro	Ala 1885		Gly	Arg	Gln	Val 1890	Thr	Val	Gln
Glu	Phe 1895		Leu	Phe	Phe	Thr 1900	Ile	Phe	Asp	Glu	Thr 1905	ГÄЗ	Ser	Trp
Tyr	Phe 1910	Thr	Glu	Asn	Met	Glu 1915	Arg	Asn	Cys	Arg	Ala 1920	Pro	Cys	Asn
Ile	Gln 1925	Met	Glu	Asp	Pro	Thr 1930		Lys	Glu	Asn	Tyr 1935		Phe	His
Ala	Ile 1940	Asn	Gly	Tyr	Ile	Met 1945		Thr	Leu	Pro	Gly 1950		Val	Met
Ala	Gln 1955	Asp	Gln	Arg	Ile	Arg 1960		Tyr	Leu	Leu	Ser 1965		Gly	Ser
Asn	Glu 1970	Asn	Ile	His	Ser	Ile 1975	His	Phe	Ser	Gly	His 1980		Phe	Thr
Val	Arg 1985	Lys	Lys	Glu	Glu	Tyr 1990	Lys	Met	Ala	Leu	Tyr 1995		Leu	.Tyr
Pro	Gly 2000		Phe	Glu		Val 2005	Glu	Met	Leu	Pro	Ser 2010		Ala	Gly
Ile	Trp 2015		۷al	Glu	Cys	Leu 2020		Gly	Glu	His	Leu 2025		Ala	Gly
Met	Ser 2030		Leu	Phe	Leu	Val 2035	Tyr	Ser	Asn	Lys	Cys 2040		Thr	Pro
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Ser	Gly 2060		Tyr	Gly	Gln	Trp 2065		Pro	Гуs	Leu	Ala 2070		Leu	His

Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys Glu Pro Phe Ser 2080 2075 Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile His Gly Ile 2095 Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr Ile Ser / 2110 2105 Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln Thr 2130 21,25 2120 Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn 2145 2140 2135 Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile 2155 2150 Ile Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg 2170 2175 Ser Thr Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys 2185 2180 Ser Met Pro Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln 2200 2195 Ile Thr Ala Ser Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser 2220 2215 2210 Pro Ser Lys Ala Arg Leu His Leu Gln Gly Arg Ser Asn Ala Trp 2235 2230 2225 Arg Pro Gln Val Asn Asn Pro Lys Glu Trp Leu Gln Val Asp Phe 2250 2245 2240 Gln Lys Thr Met Lys Val Thr Gly Val Thr Thr Gln Gly Val Lys 2260 2255 Ser Leu Leu Thr Ser Met Tyr Val Lys Glu Phe Leu Ile Ser Ser 2275 2270 Ser Gln Asp Gly His Gln Trp Thr Leu Phe Phe Gln Asn Gly Lys

2285 2290 2295

Val Lys Val Phe Gln Gly Asn Gln Asp Ser Phe Thr Pro Val Val 2300 2305 2310

Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr Leu Arg Ile His 2315 2320 2325

Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met Glu Val Leu 2330 2340

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Trp Ala Ala Ala His Ala Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr 20 25 30

Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln 35 40 45

Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys 50 55

Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp 65 70 75 80

Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys 85 90 95

Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg 100 105 110

Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu 115 120 125

Ser Lys Gln Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg 130 135 140

Pro Gly Phe Gly Val Ala Arg Pro Gly Thr Glu Thr Ser Asp Val Val 145 150 155 160

Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr 165 170 175

Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val Val Ala Ile Pro Gly 180 185 190

Asn Ala Ser Met Asp Ala Val Cys Thr Ser Thr Ser Pro Thr Arg Ser 195 200 205

Met Ala Pro Gly Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser 210 220

Gln His Thr Gln Pro Thr Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser 225 230 235 240

Phe Leu Leu Pro Met Gly Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly 245 250 255

Asp Phe Ala Leu Pro Val Gly Leu Ile Val Gly Val Thr Ala Leu Gly 260 265 270

Leu Leu Ile Ile Gly Val Val Asn Cys Val Ile Met Thr Gln Val Lys 275 280 285

Lys Lys Pro Leu Cys Leu Gln Arg Glu Ala Lys Val Pro His Leu Pro 290 295 300

Ala Asp Lys Ala Arg Gly Thr Gln Gly Pro Glu Gln Gln His Leu Leu 305 310 315 320

Ile Thr Ala Pro Ser Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala Ser 325 330 335

Ala Leu Asp Arg Arg Ala Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly 340 345 350

Val Glu Ala Ser Gly Ala Gly Glu Ala Arg Ala Ser Thr Gly Ser Ser 355 360 365

Asp Ser Ser Pro Gly Gly His Gly Thr Gln Val Asn Val Thr Cys Ile 370 375 380

Val Asn Val Cys Ser Ser Ser Asp His Ser Ser Gln Cys Ser Ser Gln 385 390 395 400

Ala Ser Ser Thr Met Gly Asp Thr Asp Ser Ser Pro Ser Glu Ser Pro 405 410 415

Lys Asp Glu Gln Val Pro Phe Ser Lys Glu Glu Cys Ala Phe Arg Ser 420 . 425 430

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ctatacagac	catctgcctg	ccctcgatgt	ataacgatcc	ccagtttggc	acaagctgtg	1020
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tgactgttgt	gaagctgatt	tcccaccggg	agtgtcagca	gccccactac	tacggctctg	1140
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<211> 431

<212> PRT

<213> Homo sapiens

<400> 34

Met Arg Ala Leu Leu Ala Arg Leu Leu Cys Val Leu Val Val Ser 1 5 10 15

Asp Ser Lys Gly Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp 20 25 30

Cys Leu Asn Gly Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile 35 40 45

His Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile 50 55 60

Asp Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly 65 70 75 80

Lys Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser 85 90 95

Ala Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu 100 105 110

- Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg 115 120 125
 - Arg Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln 130 135 140
 - Glu Cys Met Val His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro 145 150 155 160
 - Pro Glu Glu Leu Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg 165 170 175
 - Phe Lys Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp 180 185 190
 - Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val
 - Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His 210 215 220
 - Cys Phe Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly 225 230 235
 - Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val 245 250 255
 - Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His
 260 265 270
 - His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys 275 280 285
 - Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr 290 295 300
 - Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys 305 310 315

Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val 325 330 335

Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly 340 345 350

Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys 355 360 365

Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu 370 375 380

Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys 385 390 395 400

Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu 405 410 415

Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu 420 425 430

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<211> 107

<212> PRT

<213> Mus musculus

<400> 35

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Asn Thr Ala 20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile 35 40 45

Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly 50 55 60

Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Thr Thr Pro Pro

85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys 100 105

<210> 36

<211> 120

<212> PRT

<213> Mus musculus

<400> 36

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Lys Asp Thr 20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 35 40 45

Ala Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Ala Asp Ser Val

Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys 85 90 95

Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr Trp Gly Gln 100 105 110

Gly Thr Leu Val Thr Val Ser Ser 115 120

<210> 37

<211> 120

<212> PRT

<213> Mus musculus

<400> 37

Gln Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln 1 5 10 15

Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser 20 25 30

Gly Met Ser Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Ala Leu Glu 35 40 45

Trp Leu Ala Asp Ile Trp Trp Asp Asp Lys Lys Asp Tyr Asn Pro Ser 50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val 65 70 75 80

Val Leu Lys Val Thr Asn Met Asp Pro Ala Asp Thr Ala Thr Tyr Tyr 85 90 95

Cys Ala Arg Ser Met Ile Thr Asn Trp Tyr Phe Asp Val Trp Gly Ala 100 105 110

Gly Thr Thr Val Thr Val Ser Ser 115 120

<210> 38

<211> 106

<212> PRT

<213> Mus musculus

<400> 38

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Asp Arg Val Thr Ile Thr Cys Lys Cys Gln Leu Ser Val Gly Tyr Met 20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Trp Ile Tyr 35 40 45

Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser 50 55 60

Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp 65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Phe Gln Gly Ser Gly Tyr Pro Phe Thr 85 90 95

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys 100 105

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<210> 40 <211> 282 <212> PRT <213> Homo sapiens

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<213> HOMO Saprem

<400> 40

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gttcccgact cggctcttcc ctttaacttc caggctgcct atggcctgag tgaccaactg

gcccaagcca tcagtgacca ctatccagtg gaggtgatgc tgaagtgagc agcccctccc

900

960

1020

1039

5

1

10

15

Leu Gln Gly Ala Val Ser Leu Lys Ile Ala Ala Phe Asn Ile Gln Thr 20 25 30

Phe Gly Glu Thr Lys Met Ser Asn Ala Thr Leu Val Ser Tyr Ile Val 35 40 45

Gln Ile Leu Ser Arg Tyr Asp Ile Ala Leu Val Gln Glu Val Arg Asp 50 55 60

Ser His Leu Thr Ala Val Gly Lys Leu Leu Asp Asn Leu Asn Gln Asp 65 70 75 80

Ala Pro Asp Thr Tyr His Tyr Val Val Ser Glu Pro Leu Gly Arg Asn 85 90 95

Ser Tyr Lys Glu Arg Tyr Leu Phe Val Tyr Arg Pro Asp Gln Val Ser 100 105 110

Ala Val Asp Ser Tyr Tyr Tyr Asp Asp Gly Cys Glu Pro Cys Gly Asn 115 120 125

Asp Thr Phe Asn Arg Glu Pro Ala Ile Val Arg Phe Phe Ser Arg Phe 130 135 140

Thr Glu Val Arg Glu Phe Ala Ile Val Pro Leu His Ala Ala Pro Gly
145 150 155 , 160

Asp Ala Val Ala Glu Ile Asp Ala Leu Tyr Asp Val Tyr Leu Asp Val 165 170 175

Gln Glu Lys Trp Gly Leu Glu Asp Val Met Leu Met Gly Asp Phe Asn 180 185 190

Ala Gly Cys Ser Tyr Val Arg Pro Ser Gln Trp Ser Ser Ile Arg Leu 195 200 205

Trp Thr Ser Pro Thr Phe Gln Trp Leu Ile Pro Asp Ser Ala Asp Thr 210 215 220

Thr Ala Thr Pro Thr His Cys Ala Tyr Asp Arg Ile Val Val Ala Gly 225 230 235

Met Leu Leu Arg Gly Ala Val Val Pro Asp Ser Ala Leu Pro Phe Asn 245 250 255

Phe Gln Ala Ala Tyr Gly Leu Ser Asp Gln Leu Ala Gln Ala Ile Ser 260 265 270

Asp His Tyr Pro Val Glu Val Met Leu Lys 275 280

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<210> 42 <211> 226 <212> PRT

<213> Mus musculus

<400> 42

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Glu Arg Val Ser Phe Ser Cys Arg Ala Ser Gln Phe Val Gly Ser Ser

20 25 30

Ile His Trp Tyr Gln Gln Arg Thr Asn Gly Ser Pro Arg Leu Leu Ile 35 40 45

Lys Tyr Ala Ser Glu Ser Met Ser Gly Ile Pro Ser Arg Phe Ser Gly . 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Ser Ile Asn Thr Val Glu Ser 65 70 75 80

Glu Asp Ile Ala Asp Tyr Tyr Cys Gln Gln Ser His Ser Trp Pro Phe 85 90 95

Thr Phe Gly Ser Gly Thr Asn Leu Glu Val Lys Glu Val Lys Leu Glu 100 105 110

Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Met Lys Leu Ser 115 120 125

Cys Val Ala Ser Gly Phe Ile Phe Ser Asn His Trp Met Asn Trp Val 130 135 140

Arg Gln Ser Pro Glu Lys Gly Leu Glu Trp Val Ala Glu Ile Arg Ser 145 150 155 160

Lys Ser Ile Asn Ser Ala Thr His Tyr Ala Glu Ser Val Lys Gly Arg 165 170 175

Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ala Val Tyr Leu Gln Met 180 185 190

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Tyr Tyr Gly Ser Thr Tyr Asp Tyr Trp Gly Gln Gly Thr Thr Leu Thr 210 215 220

Val Ser 225

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agaa	ctac	tg c	aact	agac	g ca	gccc	gcag	gca	gccc	ccc	accc	gccg	cc t	cctg	caccg	420
agag	agat	gg a	ataa	agcc	c tt	gaac	cagc									450
1 Trp	> 1 > F > H > 4 Ala	Leu Pro	Asp 20	Met 5 Pro	Ala	Ala	Ala	Phe 25	10 Val	Asn	Ala Gln Gly	His	Leu 30	Cys	Gly	
Phe	Tyr 50	Thr	Pro	Lys	Thr	Arg 55	Arg	Glu	Ala	Glu	Asp 60	Leu	Gln	Val	Gly	,
Gln 65	Val	Glu	Leu	Gly	Gly 70	Gly	Pro	Gly	Ala	Gly 75	Ser	Leu	Gln	Pro	Leu 80	
Ala	Leu	Glu	Gly	Ser 85	Leu	Gln	Lys	Arg	Gly 90	Ile	Val	Glu	Gln	Cys 95	Cys	
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<213>
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                                                                      120
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                                                                      360
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<210> 46

<211> 400

<212> PRT

<213> Hepatitis B virus

<400> 46

Ser Val Pro Asn Pro Leu Gly Phe Phe Pro Asp His Gln Leu Asp Pro 20 25 30

- Ala Phe Gly Ala Asn Ser Asn Asn Pro Asp Trp Asp Phe Asn Pro Asn 35 40 45
- Lys Asp His Trp Pro Glu Ala Ile Lys Val Gly Ala Gly Asp Phe Gly 50 55 60
- Pro Gly Phe Thr Pro Pro His Gly Gly Leu Leu Gly Trp Ser Pro Gln 65 70 75 80
- Ala Gln Gly Ile Leu Thr Thr Val Pro Ala Ala Pro Pro Pro Val Ser 85 90 95
- Thr Asn Arg Gln Ser Gly Arg Gln Pro Thr Pro Ile Ser Pro Pro Leu 100 105 110
- Arg Asp Ser His Pro Gln Ala Met Gln Trp Asn Ser Thr Thr Phe His 115 120 125
- Gln Ala Leu Leu Asp Pro Arg Val Arg Gly Leu Tyr Phe Pro Ala Gly
- Gly Ser Ser Ser Gly Thr Val Asn Pro Val Pro Thr Thr Val Ser Pro 145 150 155
- Ile Ser Ser Ile Phe Ser Arg Thr Gly Asp Pro Ala Pro Asn Met Glu 165 170 175
- Ser Thr Thr Ser Gly Phe Leu Gly Pro Leu Leu Val Leu Gln Ala Gly 180 185 190
- Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile Pro Gln Ser Leu Asp Ser 195 200 205
- Trp Trp Thr Ser Leu Asn Phe Leu Gly Gly Ala Pro Thr Cys Pro Gly 210 215 220
- Gln Asn Ser Gln Ser Pro Thr Ser Asn His Ser Pro Thr Ser Cys Pro 225 230 235

Pro	Ile	Cys	Pro	Gly 245	Tyr	Arg	Trp	Met	Cys 250	Leu	Arg	Arg	Phe	11e 255	Ile	
Phe	Leu	Phe	Ile 260	Leu	Leu	Leu	Сув	Ьеи 265	Ile	Phe	Leu	Leu	Val 270	Leu	Leu	
Asp	Tyr	Gln 275	Gly	Met	Leu	Pro	Val 280	Cys	Pro	Leu	Leu	Pro 285	Gly	Thr	Ser	
Thr	Thr 290	Ser	Thr	Gly	Pro	Cys 295	Lys	Thr	Cys	Thr	Ile 300	Pro	Ala	Gln	Gly	
Thr 305	Ser	Met	Phe	Pro	Ser 310	Cys	Cys	Cys	Thr	Lуs 315	Pro	Ser	Asp	Gly	Asn 320	
Сув	Thr	Cys	Ile	Pro 325	Ile	Pro	Ser	Ser	Trp 330	Ala	Phe	Ala	Arg	Phe 335	Leu	
Trp	Glu	Trp	Ala 340	Ser	Val	Arg	Phe	Ser 345		Leu	Ser	Leu	Leu 350	Val	Pro	
Phe	Val	Gln 355		Phe	Ala	Gly	Leu 360	Ser	Pro	Thr	Val	Trp 365	Leu	. Ser	Val	
Ile	Trp 370		Met	Trp	Tyr	Trp 375		Pro	Ser	Leu	Tyr 380	Asn	lle	. Leu	Ser	
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CCC	aacc	att	ccct	tato	ca g	gcct	tttg	ga ca	acgo	tate	gete	cege	gccc	atco	gtctgca	180
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<210> 48 <211> 217 <212> PRT <213> Homo sapiens

<400> 48

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Cys Leu Pro Trp Leu Gln Glu Gly Ser Ala Phe Pro Thr Ile Pro Leu 20 25 30

Ser Arg Pro Phe Asp Asn Ala Met Leu Arg Ala His Arg Leu His Gln 35 40 45

Leu Ala Phe Asp Thr Tyr Gln Glu Phe Glu Glu Ala Tyr Ile Pro Lys 50 55 60

Glu Gln Lys Tyr Ser Phe Leu Gln Asn Pro Gln Thr Ser Leu Cys Phe 65 70 75 80

Ser Glu Ser Ile Pro Thr Pro Ser Asn Arg Glu Glu Thr Gln Gln Lys 85 90 95

Ser Asn Leu Glu Leu Leu Arg Ile Ser Leu Leu Leu Ile Gln Ser Trp 100 105 110

Leu Glu Pro Val Gln Phe Leu Arg Ser Val Phe Ala Asn Ser Leu Val 115 120 125

Tyr Gly Ala Ser Asp Ser Asn Val Tyr Asp Leu Leu Lys Asp Leu Glu 130 135 140

Glu Gly Ile Gln Thr Leu Met Gly Arg Leu Glu Asp Gly Ser Pro Arg 145 150 155 160

Thr Gly Gln Ile Phe Lys Gln Thr Tyr Ser Lys Phe Asp Thr Asn Ser 165 170 175

His Asn Asp Asp Ala Leu Leu Lys Asn Tyr Gly Leu Leu Tyr Cys Phe 180 185 190

Arg Lys Asp Met Asp Lys Val Glu Thr Phe Leu Arg Ile Val Gln Cys

Arg Ser Val Glu Gly Ser Cys Gly Phe 210 215

<210> 49

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tga

<210> 50

<211> 320

<212> PRT

<213> Homo sapiens

<400> 50

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Asp Ala Pro Ala Pro Thr Pro Cys Val Pro Ala Glu Cys Phe Asp Leu 35 40 45

Leu Val Arg His Cys Val Ala Cys Gly Leu Leu Arg Thr Pro Arg Pro 50 55 60

Lys Pro Ala Gly Ala Ser Ser Pro Ala Pro Arg Thr Ala Leu Gln Pro 65 70 75 80

Gln Glu Ser Val Gly Ala Gly Ala Gly Glu Ala Ala Val Asp Lys Thr 85 90 95

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser 100 105 110

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg 115 120 125

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro 130 135 140

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala 145 150 155 160

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val

175

165

170

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr 195 200 205

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu 210 215 220

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys 225 230 235

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser 245 250 255

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp 260 265 270

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser 275 280 285

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala 290 295 300

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys 305 310 315

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<211> 107

<212> PRT

<213> Homo sapiens

<400> 51

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Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Tyr 20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile 35 40 45

Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro 65 70 75 80

Asp Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp 85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Val Lys 100 105

<210> 52

<211> 107

<212> PRT

<213> Mus musculus

<400> 52

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly 1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Tyr 20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Ile Val Lys Leu Leu Ile 35 40 45

Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln 65 70 75 80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys 100 . 105

<210> 53

<211> 119

<212> PRT

<213> Homo sapiens

<400> 53

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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr 20 25 30

Leu Ile Glu Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile 35 40 45

Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe 50 55 60

Lys Gly Arg Val Thr Leu Thr Val Asp Glu Ser Thr Asn Thr Ala Tyr 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys 85 90 95

Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Gln Gly
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Thr Leu Val Thr Val Ser Ser 115

<210> 54

<211> 119

<212> PRT

<213> Mus musculus

<400> 54

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Leu Ile Glu Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile 35 40 45

Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe 50 55 60

Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Thr Thr Ala Tyr 65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Asp Asp Ser Ala Val Tyr Phe Cys 85 90 95

Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Arg Gly 100 105 110

Thr Leu Val Thr Val Ser Ala 115

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<211> 214

<212> PRT

<213> Homo sapiens

<400> 55

Asp Ile Gln Met Thr Gln Thr Pro Ser Thr Leu Ser Ala Ser Val Gly
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Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Tyr 20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile 35 40 45

Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 55

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro

Asp Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp 85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Val Lys Arg Thr Val Ala Ala 100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly 115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala 130 135 140 Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln 145 150 155

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser 165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr 180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser 195 200 205

Phe Asn Arg Gly Glu Cys 210

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<212> PRT

<213> Homo sapiens

<400> 56

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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr 20 25 30

Leu Ile Glu Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile 35 40 45

Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe 50 55

Lys Gly Arg Val Thr Leu Thr Val Asp Glu Ser Thr Asn Thr Ala Tyr 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys 85 90 95

Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe 115 120 125

- Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu 130 135 140
- Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp 145 150 155 160
- Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu 165 170 175
- Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser 180 185 190
- Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro 195 200 205
- Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys 210 220
- Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro 225 230 235 240
- Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser 245 250 255
- Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp 260 265 270
- Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn 275 280 285
- Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val 290 295 300
- Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu 305 310 315 320
- Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys 325 330 335
- Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr

340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr 355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu 370 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu 385 390 395

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys 405

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<211> 8540

<212> DNA

<213> Homo sapiens

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